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THE WAR OFFICE

Memoranda on

Medical Diseases in Tropical and Sub-Tropical Areas

Eighth Edition
1946

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THE WAR OFFICE
10th July, 1946

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PREFACE

These Memoranda were originally compiled by the late Sir Andrew Balfour, K.C.M.G., C.B., F.R.S., for medical officers serving abroad in the war of 1914-18. He and his collaborators prepared two further editions and the work continued to expand under the editorship of Lieutenant-General Sir William MacArthur, K.C.B., D.S.O., O.B.E. This, the eighth, edition contains new articles on Infective Hepatitis, Leprosy, Nutritional Diseases, Sulphonamide Drugs, Tropical Eosinophilia, and Uses of D.D.T., while the formerly separate sections on Kala-azar and Oriental sore (Cutaneous leishmaniasis) have been brought together under the single heading: Leishmaniasis. In the same way, the section on Amœbiasis includes Intestinal amœbiasis (Amœbic dysentery) and Hepatic amœbiasis (Hepatic abscess).

Many sections have been wholly or largely rewritten to bring them into line with the numerous and rapid advances in our knowledge during the 1939-45 war, and 20 new figures or plates have been added or substituted. Many of the illustrations have been lent by the Wellcome Bureau of Scientific Research.

[illegible] claim to be more than a series [illegible]

a rival, to standard works.

The task of producing a new edition has been helped forward in different ways by many friends of the War Office, and by the useful suggestions offered by reviewers who took notice of the seventh (1942) edition. We have not met all the points brought to our notice; therefore [illegible]

Alex Hood

Lieutenant-General,
Director-General,
Army Medical Services.

10th July, 1946.

ANCYLOSTOMIASIS

This important helminthic infection prevails wherever climatic conditions and imperfect sanitation permit the development of ancylostomes The disease is widely distributed between the latitudes of 30 deg N. and 30 deg. S , and beyond these limits it has been found among workers in mines and tunnels, owing to the higher temperature in such places, and the lack of sanitary control

Etiology.—Human ancylostomiasis is due mainly to two species of nematode worms belonging to different genera of the family Acylostomidæ One of these species is *Ancylostoma duodenale*, the other *Necator americanus* Their respective distribution is difficult to demarcate as they have often been confused in the past In most affected countries both species occur, and they may be present in the same person. Other factors being equal, *A duodenale* appears to be more hurtful to its host than *N americanus* *A braziliense*, *A caninum* and *A malayanum*, ancylostomes normally parasitic on animals, occasionally invade man, giving rise to a creeping eruption of the skin But these animal ancylostomes do not undergo further development in the human host , therefore visceral symptoms do not follow

The ancylostomes are small worms, about 8–10 mm long, of a pinkish-white colour when alive, but grey when dead When gorged with blood they are reddish brown Male and female forms are present and their habitat is the human small intestine, more especially the jejunum, though they are also found in the duodenum and rarely in the ileum Ancylostomes attach themselves to the mucous membrane by means of their buccal armature, more formidable in the case of *A duodenale*. Its mouth capsule possesses both dorsal and ventral hooked teeth, while in *N americanus* the solitary so-called "tooth" is dorsal The latter has the teeth proper replaced by chitinous plates Each species is also armed with internal buccal lancets

In *A braziliense*, the outer pair of ventral teeth are large and well developed, whereas the inner pair are minute

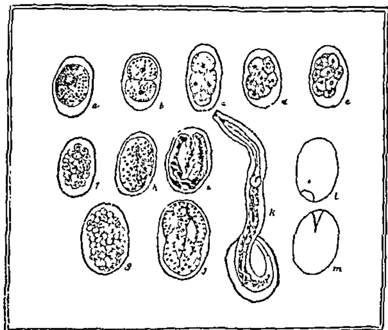
These worms are blood-sucking parasites, and the symptoms they produce are due in part to loss of blood, in part doubtless to the slow destruction of the mucosa and submucosa on which the ancylostomes feed, and possibly also to the effects of a hæmolytic toxin which they are believed to excrete It has also been said that bacterial infections may result through the lesions caused by the parasites and that these play an important part in the symptomatology.

A certain amount of development occurs as the egg travels down the human alimentary canal, for the contained granular mass divides into [illegible]

95 deg F) In twenty-four hours, if the conditions are favourable, the

young embryo can be seen coiled up in the egg. It escapes from it as a larva in from two to seven days and feeds upon the fæces (Fig. 1). The larva moults twice, and often after the second moult it retains the cast skin as a sheath, but this may be discarded. It has now reached the infective stage and, ceasing to feed and grow, it makes for moist earth or water. It is active and can swim, wriggle, and even climb up any surface which is wet, and it is greatly assisted in its progression by the presence

Fig. 1.



Development of *Ancylostoma duodenale* a b, c, d, e f, g, segmentation of egg, h, i, j, the larva, k escape of larva from egg, l, m, empty egg shell Greatly enlarged (After Perroncito)

of an accompanying film of water. Larvæ may pass vertically through as much as thirty-six inches of light soil to reach the surface of the ground, but their radial spread from a focus of infection seems to be limited to a few inches.

Infection can take place in two ways, through the mouth and through the skin The latter is much the more important, though direct trans- [illegible] which the larvæ pass, and from the subcutaneous tissues they reach the veins and lymphatics and travel to the intestine via the heart, arteries, capillaries, and air cells of the lung, bronchi, trachea, larynx, œsophagus and stomach. Leaving the stomach, they mature in the intestine, and,

after copulation, the *female* produces eggs which appear in the fæces seven to ten weeks after infection. There is evidence to show than an alternative route from the lungs is also, though more rarely, followed, namely, by the pulmonary artery to the pulmonary veins and in the general blood stream to the jejunum, where the mucosa is pierced and the larvæ reach the lumen of the bowel.

The adult worms may remain alive in the intestine, in diminishing numbers, for as long as six years.

Symptoms.—As the ancylostomes present vary greatly in numbers the symptoms naturally also vary in different cases. Other factors in variability are personal idiosyncrasy and the presence of associated diseases. In the main the symptomatology is that of a secondary anæmia Recent studies have shown the importance of a deficient diet in the production of this anæmia

There are cryptic, mild, and severe types. In the first variety the disease can only be definitely diagnosed by the finding of ova in the stools. Such cases are rather ancylostome carriers than victims of ancylostomiasis, but careful inquiry will often show some slight digestive trouble with tenderness and pain and discomfort in the epigastrium. There may be a slight reduction in the hæmoglobin content of the blood and a trifling loss in the power of mental concentration It may be said of such cases that they do not know they have been ill until they are cured They notice the difference in their health when freed from their worms. A blood examination may reveal eosinophilia and suggest an examination of the fæces It has been stated that 500 worms must be present for six months before effects are produced on the host

The mild cases present moderate anæmia, and epigastric tenderness is a marked feature often associated with acid dyspepsia. The ingestion of food frequently, if temporarily, relieves the painful sensations. Palpitation, tachycardia, pulsation of neck veins, and a low systolic blood pressure are among the commonest cardio-vascular symptoms. Cough and bronchitis may occur, due possibly to passage of the larvæ through the lungs

Severe cases show a disordered or depraved appetite. It is often ravenous, and a craving for earth is common. The patient becomes pot-bellied, his stomach may be dilated and he is usually constipated. Rarely there is blood in the stools mixed up with the fæces.

Physical and mental fatigue ensue, together with various nervous symptoms and joint pains As the anæmia progresses the palpitation and dyspnœa increase In marked cases the red cell count may be as low as 2 million per c mm with a hæmoglobin of 20 per cent Œdema shows itself in advanced cases chiefly about the face and ankles, a puffy face is not uncommon and ascites may occur The patient rather resembles a man suffering from chronic nephritis. In white patients the skin, which is dry, assumes an earthy hue, and attention has been drawn to the peculiar dead-white appearance of the conjunctiva of the lower lid, and to the pale flabby tongue which has been likened to white blotting-paper.

It is important to note that ancylostomiasis may apparently be a cause of jaundice and of liver enlargement There is no change in the spleen

Emaciation is not a feature of the disease in adults. Stunting, both mental and physical, is common in children with severe parasitization. Faulty *nutrition is usually* an important factor in these cases.

So much for the general symptoms. In the tropics anæmia plus dropsy should always lead one to think of ancylostomiasis. As regards the skin eruption at the site of invasion, it suffices to say that at the start it is a mild dermatitis characterized by redness and the presence of urticarial weals or small vesicles, and that later, owing to secondary pyogenic infection, it assumes a pustular character. It is known as ground-itch It should be noted that the skin invasion by *A. duodenale* does not always give rise to dermatitis and that ground-itch is not common in Egypt where ancylostomiasis is rife.

Complications.—Ulceration of the mouth may be noted. The disease *often occurs along with malaria and amœbic dysentery.*

Diagnosis.—This can only be made with certainty by the discovery of ova in the fæces, though it must be remembered that their absence does

plan to place washed and sedimented fæces on a slide for a few minutes and then gently immerse in water. The ova remain after everything else has been washed off, and by repeating the process quite a collection of eggs may be obtained on the slide.

The eggs of such nematodes as *Trichostrongylus colubriformis* and *Ternidens deminutus*, which occasionally parasitize man, may readily be mistaken for those of ancylostomes. In doubtful cases a series of eggs should be measured, and the degree of development in the yolk of freshly passed specimens carefully noted.

Eosinophilia is often present but it is not sufficiently characteristic of the disease to be of much diagnostic value. It is often absent in severe infections and when the hookworm disease is complicated by malaria or kala-azar.

Differential Diagnosis.—Distinguish from Bright's disease, beriberi, and secondary anæmia from other causes.

Prophylaxis.—From what has been said it must be evident that the chief prophylactic measure consists in preventing the fæcal contamination of soil, water, or such foodstuffs as vegetables which are eaten uncooked. Special care as regards conservancy methods in the tropics is therefore of prime importance.

The employment of the deep bore-hole latrine affords an adequate method for disposal of fæces, and is preferable to trenching systems. In either case care must be taken to see that the edges of surfaces around the latrine openings are kept clean and that the feet of users are protected.

Bucket-removal systems are less satisfactory but may have to be employed under certain circumstances. Cresol should be placed in the latrine buckets in the usual way or, if this is not available, a layer of common salt on the bottom of the bucket and another on the top when

the bucket is full, will serve the same purpose In the latter case intimate contact with the fæces must be ensured by mixing, as solid salt does not penetrate fæces for some forty-eight hours.

If incineration is employed there must be no mixing of the fresh fæces with bhoosa or other combustible matter on the ground, thereby increasing the risk of soil contamination. From the pan to the fire must be the motto

Contaminated soil is the most important source of infection, and such contamination may be direct or indirect, the latter often occurring owing to dissemination by footwear. Over three hundred larvæ have been recovered from the muddy shoes of one person. Ova, too, may pass unaffected through the stomach and intestine of the domestic pig and may be disseminated in this way.

Camping sites must be carefully selected and kept clean. Contamination of ground may be established by the finding of larvæ and an apparatus for their detection has been devised. It consists of a funnel covered by a fine mesh sieve in which the soil is placed When the funnel is filled with water up to the lower soil level the larvæ pass into the water and can be recovered from the lower end of the funnel.

Badly contaminated ground should be abandoned, but as most of the [illegible]

measures are impossible the suspected ground may be "fired" before use.

Owing to the need of the larvæ for moisture the drying up of damp areas by drainage often achieves good results.

Water supplies should be protected and bathing places properly chosen and regulated, while all measures necessary must be taken to prevent contamination of foodstuffs such as vegetables and fruits which are eaten uncooked As a further protection all uncooked fruit and vegetables should be thoroughly washed before eating Hands should also be thoroughly washed with soap and water before, and preferably also after, all meals

Great importance is attached to the effective purification of water supplies, especially by filtration.

The protection of the individual must be given careful consideration. Boots and sandals, if not defective, protect to a great extent, but it must be remembered that when not on the march native troops may discard their boots and in this way convey infection.

Many Indian and African troops already suffer from mild degrees of [illegible]

worms. Another method is to give the oil in one single dose of 2 c cm, followed by a saline purge as before.

Oil of chenopodium is effective against *Ascaris* and *Strongyloides*.

Narcosis and other ill-effects have followed the administration of the oil and cumulative effects have been noted, so it must be given with care, especially in debilitated persons. The treatment should not be repeated under ten days. There is no chemical antidote. In cases of poisoning digitalis and adrenaline have been found useful. Caffeine does harm.

Oil of chenopodium may be combined with carbon tetrachloride, one part of the former to two of the latter. 0·1 c cm. of the mixture is given for each year of age up to 1 5 c cm The dose is divided into two equal parts taken in water at an interval of one or two hours. Two hours after the second dose a saline purge is given.

Hexylresorcinol, prescribed in gelatine capsules, has been recommended, especially in the case of critically ill patients, as it is less toxic than carbon tetrachloride. The adult dose is five pills, each containing 3 grains, taken in one dose. No food should be allowed for at least four hours after taking the drug A saline purge should be given twenty-four hours later

Remember that the passage of worms after anthelmintic treatment is an indication for continuing rather than stopping treatment. Cessation of treatment should depend on the disappearance of symptoms and the negative results of later microscopical examinations.

The anæmia must be treated by iron and other tonics, a nutritious and easily assimilable diet should be prescribed.

Ground-itch is best treated by an ointment containing zinc oxide and salicylic acid Bad cases may require antiseptic dressings.

SOME
ARTHROPOD PESTS*
WINGLESS PESTS

Under this heading the following arthropods are included :—Lice, Bugs, Fleas, the Itch Mite, Ticks and Ants

LICE

The lice comprise two groups of insects -

1 The biting or feather lice (*Mallophaga*), which live on the skin of birds and of certain non-human mammals Their mouth parts are adapted for biting solid objects

2 The sucking lice (*Anoplura*), of which only one family, *Pediculidæ*, infests man and monkeys. The members of this group have eyes and this distinguishes them from all other *Anoplura*

Animals which are closely related tend to have similar or identical lice.

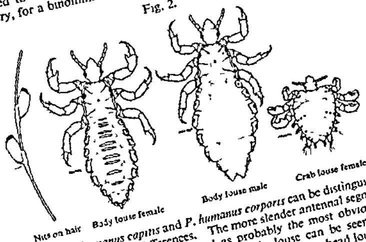
* Some of the drawings illustrating this section are reproduced by permission of the Wellcome Bureau of Scientific Research Others were drawn from life by John Hull Grundy

The family *Pediculidæ* comprises three genera: *Pedicinus*, *Pediculus*, and *Phthirus*. Of these, *Pedicinus* is found only on monkeys; *Pediculus* and *Phthirus* infest only man and the higher apes—they do not infest other monkeys.

The sucking lice are markedly host-specific, living only on one host or on a few that are closely related. They are also obligate parasites, living their whole lives on the skin of their chosen mammal. As far as we know, they have few enemies in nature. They can harbour the spirochætes of relapsing fever and the rickettsiæ of typhus and trench fever.

The genera of which man is the natural host comprise two species, *Pediculus humanus* (head and body lice) and *Phthirus pubis* (crab lice) (Fig 2) Head lice and body lice are now regarded as varieties of *Pediculus humanus*, and not as two distinct species. Consequently, if it is desired to separate these two sub-species a trinominal designation is necessary, for a binominal label is the badge of a species.

Fig. 2.



Usually *P. humanus capitis* and *P. humanus corporis* can be distinguished by slight morphological differences. The more slender antennal segments of the body louse may be mentioned as probably the most obvious of these. The third antennal segment of a body louse can be seen at a glance to be definitely longer than it is broad, whereas in a head louse the broadest part of this segment is not strikingly less than the length. Head lice are usually somewhat smaller and more deeply pigmented than body lice, indentations between their successive abdominal segments are also deeper and more clearly marked, and their legs are somewhat shorter. These variable factors are useful enough as generalizations but of little diagnostic value in any particular case.

Biological differences are of more importance. Head lice attach their eggs to hair whereas body lice attach them to the inner side of clothing in close contact with the body. On account of their environmental conditions, head lice are more active at low temperatures than body lice; but the distinction between the two is far from sharp. Head lice may often be found on the body; less often body lice are found on the head. It may be assumed that a certain amount of inter-breeding takes place; this

would account for individuals with features common to both It has been asserted that lice from Europeans, Africans, Chinese, and other races show slight and inconstant differences, and that lice which infest dark skins are themselves more pigmented than those from fair skins.

Diseases transmitted by lice.—Epidemic typhus, epidemic relapsing fever, and trench fever Lice cause considerable cutaneous irritation, and as a result of scratching, secondary infection may occur, and diseases such as impetigo, infective dermatitis, and furunculosis may develop in infested persons Until these complications develop, general symptoms of toxæmia due to the actual infestation are not usually noted, but if a patient is very heavily infested, general symptoms of a toxic nature may be seen there is usually a slight but persistent rise of temperature, headache, lethargy, and pains in the joints, and a rash resembling german measles may appear. These symptoms disappear when the patient is deloused.

As far as we know, the crab louse (*Phthirus pubis*) transmits no specific disease, but it irritates the skin, and the consequent scratching leads to infection

PEDICULUS HUMANUS CORPORIS

Under ideal conditions the female body louse may lay 10 eggs a day, and a total number of about 300 in the course of her life. Egg-laying is most active at a temperature of 30° C. (88° F) and ceases at 20° C. (68° F) If kept at body temperature (37° C.) the eggs hatch in about six days , at temperatures above 37° C. (98 6° F.) eggs do not develop, and are killed if a temperature of 40° C. (104° F) is maintained Under cold conditions eggs are killed in two hours at a temperature of—17° C. (1 4° F), and in seven days at a temperature of 5° C. (41° F). If maintained at a temperature of 22° C. (72° F) ova do not hatch The development of the ova may be retarded by variations of temperature and if infested clothing is not worn frequently the hatching may be delayed for as long as 25 days

The larva which emerges from the egg has a [illegible] development —

> The egg stage lasts nine days and 30 per cent of the eggs fail to hatch The larval stage lasts for nine days and the mortality may be 40 per cent. The female lives for 34 days , she does not lay eggs on the 1st, 2nd or 34th day, but she may lay nine eggs a day from the third to the thirty-third day inclusive, *i e* a total of 279 eggs Therefore, allowing for the mortality of eggs and larvæ, 100 eggs produce 42 adults.

The geographical distribution of lice is very wide, and there is no part of the world in which the insect (either *corporis* or *capitis*) cannot be found, except for a few localized areas where the inhabitants have maintained a high standard of personal hygiene At ordinary room temperatures (*e g.* 16° C., 61° F) in temperate climates they can exist without feeding for a week, but in warmer climates their life is shortened and at temperatures of 30° C. (86° F.) they usually die in two days if removed

om their host. Infestations can therefore easily arise from sleeping on raw or blankets where a lousy individual has slept a few days previously. t is important to remember that fluctuations in temperature retard the development of the eggs and that, even in a temperate climate, eggs on clothing may remain a possible source of infestation for about 25–30 days, which is approximately the limit of life in the egg.

Severe infestations readily occur in those who have to wear their clothes continuously. It should be noted that lice tend to leave their host if he has a fever or if his temperature falls at death, and thereby epidemics of louse-borne diseases may occur.

Examination for lice.—Persons harbouring body lice usually have scratch marks scattered on the body, particularly on the shoulders and waist. The actual bites of the insect may be seen as tiny punctures with an encircling area of erythema; the clothes should be carefully searched, particularly the under-garments, with special attention to the seams and folds, for it is here that the eggs will be found. Sometimes body lice may be found on the skin and in the bedding of infested persons. The eggs are the size of a pin's head (0·8 mm. long by 0·3 mm. broad), yellowish white in colour, goblet-shaped, and firmly attached at the lower end to the cloth fibre by a cement secreted by the female at the time of laying.

Lice are very susceptible to rises or falls of temperature and will readily leave a typhus patient with high fever; as a result there may be a fev adult lice but many nits on his clothing. Lice may be passed from perso to person by close personal contact as in the case of troops on acti service or refugees huddled together for warmth.

Lice may pass from their host on to chairs or bedding, and they may become airborne, especially the younger forms, when infested bedding anc clothing is handled or shaken. Therefore in making an examination b careful to stand to windward of the clothes and person examined.

Preventive Measures

1. Sources of infestation should be avoided; this is very important and soldiers should be discouraged from mixing with an infested local population, particularly if typhus is prevalent.

2. Frequent bathing and washing of clothes will remove adult lice that may be picked up. At least one hot bath and one change of underclothing should be provided each week, if possible.

3. If conditions favour infestation, and bathing and laundry facilities are poor, it is desirable to issue an anti-louse powder. The best is 10 per cent. D.D.T. in some inert powder such as kaolin. The amount required is about ¾ oz. a person a week; the individual himself sprinkles the powder on the clothing and rubs it into the seams.

4. Clothing impregnated with a persistent insecticide such as D.D.T. gives almost complete protection. This is the principle of "anti-typhus" shirts (shirts A/T).

5. Self-inspection is important if conditions favour lousiness. Underclothing should be carefully looked over each time it is removed.

6. Every soldier joining a new unit should be inspected to ensure that he is not introducing lice.

7 Periodical inspections are required to ensure that the unit is free from infestation and to pick out verminous individuals who might infest others. The intervals between inspections will depend on the risks of infestation ; if there is typhus in the district they should be held weekly. For the inspection, all should be completely stripped and examined in a good light, underclothing must be thoroughly examined at the same time.

8 Men found with lice should be disinfested as early as possible to prevent spread of the infestation, the larger the number of infested men deloused at any one time, the fewer the verminous companions to infest the remainder.

9 The hair should always be kept short, especially at the back and sides of the head

DESTRUCTION OF LICE

Lice can be destroyed by insecticides or steam. As far as the British Army is concerned, steam disinfectors are now used only for the clothing and other effects of typhus patients and contacts

Insecticides.—At present D D.T (dichlor-diphenyl-trichlorethane) is used ; it can be applied either as an emulsion for impregnating garments, "anti-typhus shirts" (shirts A/T) for example, or as a dust for puffing under the clothes. If a shirt A/T is washed not oftener than once a week, it will kill lice that come in contact with it for up to six weeks, thereafter the shirt needs re-impregnation. To dust clothes, anti-louse powder is blown between the under surface of the clothing and the skin and into each layer of clothing by means of a dust-gun, the nozzle of which is pushed under the clothing. The following details should be observed —

1 Remove the hat ; blow powder on its under-surface, replace the hat on the head
2. Open the neck of the tunic at the front and blow powder first into the right armpit, then into the left armpit, and finally straight down
3 With both arms held straight out to the side—to remove all obstruction—blow powder first down the right sleeve and then down the left sleeve
4. Insert the nozzle at the top of the trousers in front; blow powder first down the right leg and then down the left leg
5 Insert the nozzle at the top of the trousers behind and blow powder straight down.
6. Finally insert the nozzle at the back of the neck and blow powder straight down.
7 Spare clothing and bedding should be folded and the powder blown between adjacent folds.
8 The process should be repeated after two weeks because nits are not destroyed and it is essential to ensure sufficient concentration to kill young lice as they hatch out.

The advantages of this method are that the dusting can be carried out quickly—about two minutes for each person ; that the effect is persistent, particularly if the clothing is not removed for some time after ; and that bathing is not necessary. It is a very suitable method for dealing with

large numbers. Its disadvantage is that it does not disinfect; therefore the clothing of typhus patients and contacts must be sterilized by steam.

Steam.—Lice and eggs are readily killed by exposure to a temperature of over 80° C. (176° F.). This is most conveniently obtained by low pressure steam.

Low-pressure steam.—Downward displacement of air is the principle involved. Steam passing into the top of the chamber displaces air downwards; *usually 10–20 minutes should be allowed after all the air has been* displaced. After the first steam appears at the outlet, some time must still elapse before all the air has been displaced, especially from the centre of a bundle of clothes. Displacement is complete when a full-bore jet of steam (steam unmixed with air) issues from the outlet.

Clothes should be packed evenly and tightly into the disinfecting chamber to prevent steam from side-tracking through crevices. To ensure drying, clothes should be well shaken as soon as they are taken out of the chamber. This is the mode of action of the Field Portable Disinfectors numbers 2 and 3 and the Serbian Barrel. The method is used only when there is need to sterilize as well as disinfest the clothing, as in typhus patients and contacts. It cannot be used *for waterproofed*, rubber, or webbing articles, for leather articles such as boots, or for [illegible] (A/V) battle dress. It also spoils gloves and buttons and it [illegible]

can easily be scraped off.

These points should be borne in mind:—

1. The staff employed in delousing and disinfection should be permanent, specially instructed, and trustworthy. They should be fully [illegible]
2. [illegible]
3. [illegible] not on both simultaneously.
4. Clean and disinfested articles *of clothing should not be stored*, even temporarily, where infested articles have been kept. Until disinfested, vehicles used for the conveyance of dirty articles should not be used for clean articles.
5. Units should be disinfested as a whole and at the same time in order to prevent those not yet deloused from re-infesting those who have been.

PEDICULUS HUMANUS CAPITIS

In almost all points of its life-history *P. humanus capitis* resembles *P. humanus corporis* (Fig. 2). The head louse is normally confined to the more hairy parts of the body, particularly—as its name indicates—the head.

The eggs, usually called "nits", are generally laid on the inch of hair

nearest the skin, and are firmly attached to individual hairs by a cement secreted by the female louse. The egg cases remain firmly attached to the hairs when the young lice have hatched out and as the hair grows they become increasingly conspicuous. The application of vinegar or 10 per cent. acetic acid to the hair before it is washed or combed will help to dislodge the nits.

Prevention.—*The hair should* be kept as short as possible. If there is a high risk of infestation the scalp should be shaved—a precaution frequently adopted by Russians, Poles, and others who have learned its value. The hair should be washed frequently, a weekly washing will at least limit the intensity of infestation to moderate degree.

Destruction—Application of D.D.T. as an anti-louse powder to the [illegible]

carbolic acid (1/40) in water, olive oil and kerosene, equal parts, and methylated spirit (1 in 7) in water. The hair should be well soaked in the solution and wrapped in a towel for a couple of hours, it should then be combed with a "nit-comb".

PHTHIRUS PUBIS

Phthirus pubis (the crab louse) has much the same life-history as *Pediculus humanus*. Its usual habitat is the hair of the pubic and perianal regions but it may be found in other places on the inner and back part of the thighs, even as far down as the knees in hairy individuals; on the lower abdomen, in the axilla, and even on the eyebrows, eyelashes, and head. It is a much-flattened creature and the two hinder pairs of leg claws are particularly well developed, giving it the appearance that has led to its popular name of crab louse (Fig. 2). It is much less mobile than *Pediculus humanus* and does not, as far as we know, transmit any disease. Infestation by this parasite causes intense irritation, the bites, being confined to a limited area, may lead to inflammation which is made worse by scratching. If the eyelashes are involved there may be marginal blepharitis.

The louse itself, being almost transparent, is rather more difficult to see than *Pediculus* but the eggs are easily seen. The presence of pale bluish slatey-grey spots (maculæ ceruleæ) on the skin of the lower abdominal wall above the pubic area usually denotes a heavy infestation. This appearance must not be mistaken for the rash of typhus which it may closely resemble.

Prevention.—Since the mixing of underclothing and the communal use of latrines are probably the usual means of transmitting the crab louse, clothing should be washed regularly and latrine seats scrubbed daily. Periodic inspections and treatment of those infested will help to control infestation.

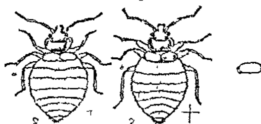
Destruction.—Insecticidal powder such as D.D.T. is dusted on the affected parts though it may cause skin irritation. Dusting has to be repeated to catch the young lice after they hatch out. Shaving the

affected parts, followed by a good wash with soap and water, is probably the best method of treatment. The perianal hair must not be forgotten. Application of mercurial ointment is said to be effective but this should not be necessary if shaving and washing have been properly carried out. For infestation of the eyelashes and eyebrows, vaseline and yellow precipitate (1 in 50) are specially recommended; the creatures can also be removed with tweezers.

THE BED-BUG

Two species of bed-bug are important: Cimex lectularius and C. hemiptera (=rotundatus) (Fig. 3 *a* and *b*). Both are brown, wingless insects almost identical in appearance; when unfed they are flat. Both have much the same habits and life history, but *C. lectularius* is the common bed-bug of northern latitudes and *C. hemiptera* is the bed-bug of the tropics.

Fig. 3.



a *Cimex lectularius*, the common bed-bug of the temperate zone
b *Cimex hemiptera*, the bed-bug of the tropics
c Bed-bug egg

Diseases transmitted by bed-bugs.—None definitely known, but the

most people.*

Habits.—Both males and females suck blood. They usually bite at if the

Bed-steads, whether of wood or iron, are favourite resting-places. They may also be found in any piece of furniture, in fittings of rooms, and above all in joints and crevices.

A hungry bug can move with surprising speed but one that has recently fed is slow because of distension. Bed-bugs can migrate from building to building and from tent to tent. They are often carried long distances in the rolled-up shirt sleeves of tropical kit; sometimes they have first been brought into a room in second-hand furniture.

Bugs are apparently more numerous in cold than in hot climates, but they are always most active and most in evidence during the summer months. Mature bugs can resist temperatures below freezing for a con-

* Flea bites and bug bites are relieved by a few applications of the following *inflammable* lotion Ichthammol *half-a-drachm, Ether to half-an-ounce.*

siderable time, but eggs and larvæ are not quite so hardy. A bug that has fed will survive without another blood-meal for nine months or more if it has no chance to feed in the interval.

Reproduction.—The female lays a large number of eggs; one female in captivity has laid as many as 111 in 81 days

[illegible]

In from four to nine days larvæ hatch out and feed soon afterwards if a blood meal is available. Four or five days thereafter the larvæ moult for the first time and attain the first nymphal stage. After four subsequent moults the adult stage is reached in about six or seven weeks from the hatching of the egg. Sexual maturity is attained about a fortnight later. In an unfavourable environment the time needed for the full cycle of development may be much prolonged.

Examination for Bed-bugs.—Joints of bedsteads, bedding (particularly "biscuits"), and mattresses should be inspected. Cross-bars and the corners of mosquito nets are favourite haunts. All furniture, walls, and fittings such as wooden skirting and window-frames, should be included in the search A not uncommon hiding-place is a kit-bag or valise.

Eggs and the black stains of bug excreta are often more obvious than the bugs themselves. Cast moults may also be prominent. To clinch the evidence, adult bugs may often be "winkled out" with a pin from holes in wall-plaster or furniture.

Routine Preventive Measures

1. Examination for bed-bugs (*see* above) should be carried out weekly at a fixed time in working hours by the whole unit under the supervision of a N.C O.

2. Iron bedsteads should be disjointed and the flame of a blow-lamp played over the component parts.

3. It is important to deny bugs harbourage by efficient maintenance of walls and fittings Cracks should be filled with cement or putty and walls should be well pointed and kept free of dust and cobwebs in which bugs often hide.

Destruction of Bed-bugs in Quarters

Two methods of destruction are of value residual spraying with D.D T. and fumigation.

D.D.T. residual spray (*see* Appendix I).—This is most effective. The following points need attention —

1. The strength is 5 per cent. D.D.T. in kerosene.
2. Use 1 gallon for each 100 square feet of surface to be sprayed.
3. Apply the spray to walls, floors, and furniture. A useful plan is to put the beds against a wall and, in one operation, spray the bed, the wall behind it, and the floor it stands on.
4. Spray mattresses separately on both sides.

5. After treatment do not allow the floor to be scrubbed. It may be swept and dusted at any time and washed five days after spraying.
6. This treatment is effective for six months but routine preventive measures must not be slackened.

Fumigation methods.—These may have to be used if D.D.T. is not available for any reason. The following are effective:—

1. Fumigation with sulphur dioxide by burning sulphur or the proprietary form of sulphur called "CIMEX".
2. Fumigation with heavy naphtha gives good results.
3. Fumigation by hydrocyanic acid gas is effective but very dangerous to carry out; it should be done only by experts

Eggs are not destroyed by fumigation; therefore a second fumigation should be done ten days after the first in order to kill off young larvæ that have hatched out in the meantime.

In carrying out methods for destruction of bed-bugs, it is of the greatest value to enlist the help and guidance of a Field Hygiene Section or Field Sanitary Section. After treatment has been carried out, the occupying *unit must not slacken routine measures for prevention.*

Reduviid Bugs.—Among this large family are a few blood-sucking parasites which act as vectors of the South American trypanosome, *T. cruzi*, the causative agent of South American trypanosomiasis (Chagas' disease). They are nocturnal biters and have a special preference for infants and young children; their bites are relatively painless. *Triatoma megista* is the most common vector of *T. cruzi* in Brazil; other known vectors are *T. infestans* (S. Brazil, Chile, Bolivia, Argentine) and *Rhodnius prolixus*.

The opossum, armadillo, and certain species of bats act as natural animal hosts of *T. cruzi*. In adults Chagas' disease usually causes little *constitutional disturbance, but in infants and young children it may be* acute and even fatal. Œdema round the eyes is an early manifestation. The mode of transmission is still in dispute.

FLEAS

Fleas are brown wingless insects, markedly flattened from side to side. (*See* Fig. 4)

Fleas and their habits.—*Pulex irritans* is the only flea of which man is the normal host, but many species normally parasitic on other animals [illegible]*

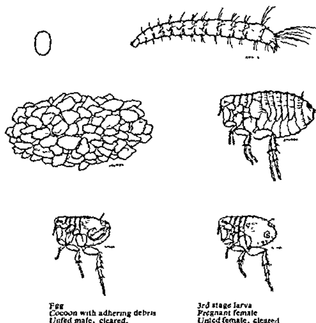
Europe, Egypt), *C. acutus*, *Hoplopsyllus anomalus* (squirrels; U.S.A.), *Stivalius ahalæ* (rats, S.E. Asia, China, Japan, etc.); *Ctenophthalmus agyrtes* (field mice; Europe); *C. canis*, *C. felis* (dogs and cats; Europe,

* For relief of irritation from flea bites, *see* footnote, page 18.

[illegible] Europe, Asia, Africa),

(rodents, Manchuria), *Pulex irritans* (man, cosmopolitan).

Fig. 4.—The Plague Flea, *Xenopsylla cheopis.*



It is interesting to note that *Leptopsylla segnis* was the flea most often found on rats in Middle-East surveys, it seldom feeds on humans and is not, therefore, regarded as an important vector of plague from rat to man

Animal fleas spend more time actually on their hosts than *Pulex irritans* spends on man Fleas always leave a dead host and they are killed off in great numbers when the temperature reaches 80° F or higher. If the raised temperature coincides with an excessive fall in atmospheric humidity the mortality is even higher. Fleas heavily infected with plague bacilli are very quickly killed off by such atmospheric conditions, because their wholly or partially blocked proventriculi are ill suited for ingestion of blood and the fleas are thus very liable to suffer dehydration even in a moist atmosphere.

Cheopis index—It is generally accepted that if rat survey reveals an average count of five *X cheopis* per rat, conditions are favourable to the spread of epidemic plague among the neighbouring human population. This figure for the average number of fleas on a rat is known as the

"cheopis index" and many plague workers attach great importance to it as a pointer to an epidemic.

Reproduction.—Whatever their normal host, all fleas breed in dust or on the ground and not on the host itself. The female lays eggs singly; these, when laid, fall to the ground. They are found most readily in dust in the sleeping-places of animals.

A larva hatches out from the egg; in summer this happens in from two to four days, but in winter it may be delayed up to 14 days. The larva is dirty white in colour, and footless but active. It is sparsely covered with long fine hairs. During this feeding stage it lives on organic matter such as flea fæces, and it is found in dust, particularly on the floors of dark passages or cellars

After about two weeks the larva attains its full size, finds a quiet and preferably dark place, and spins a cocoon, inside which it undergoes pupation. The pupal stage extends over two weeks; then the pupal case bursts and the adult flea emerges. Pupæ often seem to hatch out when mechanically disturbed—by a nearby human footstep, for example.

These usual periods are subject to great variations, and, in the case of *X cheopis*, Bacot showed that the larval stage may last from 12 to 84 days and the pupal stage from seven to 182 days.

Inspection for Immature Forms.—Dust from the floors of suspected places should be swept up and examined with a hand lens; eggs, larvæ, and pupæ are easily visible by this method.

The Flea as disease vector

Fleas are concerned in the transmission of :—

Plague.—From rat to rat, rat to man, and possibly man to man (*see* Plague).

Murine typhus.—From rat to rat, and rat to man (*see* Murine Typhus).

Helminthiasis.—*Hymenolepis diminuta*, a tapeworm of rats, and *Dipy*-

the alimentary tract of the larval flea. The larval worm passes through the mid-intestine into the hæmocele of the larval flea, from there it is carried over through the pupal stage to the adult form of the flea. The adult flea thus contains the larval stage of the worm. Such worm-infested fleas may be ingested accidentally by man, either by eating sticky fruits to which fleas are stuck or by drinking milk in which they have drowned. The larval worm is liberated by the crushing or digestion of the fleas, and the adult form of *H. diminuta* or *D. caninum* develops in the human intestine.

Preventive Measures against Fleas

1. Floors should be made of hard materials such as wood, tiles, or

concrete. Dust is easily seen on such surfaces, and they can easily be brushed down or washed; breeding is thus prevented.

2. Sandy floors of tents should be saturated with water, preferably sea- or salt-water, and stamped down hard. This makes a hard and moist floor, unsuitable for flea breeding and hard enough to stand up to brushing

3. Anti-louse powder (10 per cent. D.D.T.) should be liberally sprinkled on floors, bedding, and bed-clothes.

4. Domestic pets should be washed often with soap and water, and, if heavily infested, dusted with anti-louse powder (10 per cent. D.D.T.). The smallest dose necessary to ensure even distribution in the fur should be used and the application should not be repeated for at least 14 days. Dog kennels should be treated with D D T. residual spray (*see* Appendix I).

5. Rats and mice, which carry fleas particularly dangerous to man, should be kept down at all times by anti-rodent measures

6. Regular airing of bedding and its exposure to sunlight is important. Do not forget that a tablet of soap wielded by hand is an excellent method of catching fleas.

7. Good lighting of all buildings and tents is important

8. Protective clothing, puttees, gloves, and so forth, should be worn by all who are specially exposed to infestation.

Destruction of *Fleas*

1. D.D.T. residual spray applied to floors, furniture and the lower 3 feet of walls is very effective against fleas. Corners and obvious rat-runs should have special attention (*see* Appendix I).

2. Liberal quantities of anti-louse powder (10 per cent. D.D.T.) should be blown down rat-holes.

3. During an outbreak of plague a D D T. and cresol emulsion should be used as a disinfectant and insecticide spray Two ounces of D.D T. should be dissolved in four ounces of warm cresol and this concentrate added to a quart of water immediately before use on floors, walls, and furniture.

THE ITCH MITE

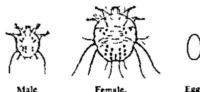
and infestation usually occurs during a period of close bodily contact.

It is disputed whether scabies is transferred from host to host during the larval or nymphal stages of the parasite's life, or whether the infestation is commonly due to migration of the adult fertilized female In all

stages the parasite prefers to live on skin and although infestation by fomites is a possibility, scabies is usually acquired by bodily contact.

Copulation in sarcoptic mites has not actually been observed and it is disputed whether this takes place in the burrows or on the surface of the skin. If the act is performed on the surface it is probably true—as has often been assumed—that the fertilized female moves on the skin until she finds a site suitable for burrowing, she appears to prefer an area where the skin may at times be lax and where small folds may be formed. The usual sites for scabies are the hands and wrists—particularly in the webs between the fingers and on the front of the wrist joint—the extensor aspect of the elbows, the anterior fold of the axillæ, the edge of the navel, the penis, the scrotum, the buttocks, the ankles, and the feet. In one series of 886 soldiers examined by Johnson and Mellanby, 63 per cent. of the mites were found on the hands and wrists, 11 per cent. on the elbows, 9 per cent. on the feet, 8 per cent. on the genitals, and 4 per cent. on the buttocks.

Fig. 5.—The Itch Mite, *Sarcoptes scabiei*.



The mite burrows in the horny layer, the rate of burrowing varying between 0 5 and 4 5 millimetres a day. She does not voluntarily leave her burrow, but lays her eggs there at the rate of two or three every twenty-four hours until some 40 or 50 have been laid, and dies after six or seven weeks Larvæ emerge from the eggs The life cycle may be summarized as follows :—

Egg stage	2½ days or more.
Larval stage	1½ to 3 days.
Nymphal stage	1½ to 2½ days.
Immature female . . .	2 to 4 days.

The nymphal stage is terminated by a moult, when either an adult male or an immature female is formed The latter has to moult once again to produce an adult female. The shortest period which elapses from the deposition of the egg to the emergence of the adult female may be less than eight days.

The larvæ leave the parent burrow, crawl over the skin and make small peri-follicular borrows. The nymphs also make little burrows and the males lie either on the surface or in small "pockets" in the epidermis. Probably it is only the adult oviparous female which makes the classical

[illegible]

[illegible]

[illegible]

female parasites, say five or under, it is most unlikely that he will transmit

... to someone who sleeps with him regularly. *Individuals*

any individual is the total number of adult female parasites which can be extracted from his skin on a single occasion, its accurate assessment is not a matter for the unskilled But if, in dealing with a scabies epidemic, careful examination shows that the parasite-rate of an adequate sample of the infested population is low, the measures taken to combat the epidemic—particularly with regard to disinfestation of fomites—need not be so vigorous as if the average parasite-rate is high

Itching does not occur until the infested person becomes sensitized to some substance (the saliva ?) produced by the mite, therefore the host's reaction to his first infestation is entirely different from that evoked by a subsequent infection During the first month of the first infestation few symptoms are noticed, transient irritation may occasionally be experienced, *but there is not any erythema at the sites of the burrows.* After a month, in the majority of cases, symptoms begin to be noted, after about six weeks the irritation is sufficient to disturb sleep, and the pruritus characteristic of clinical scabies has developed. After fourteen weeks the itching is almost continuous and nearly unbearable If, after sensitization has been established, the patient is treated and cured, and at some later date is again infested, he experiences *intense irritation* within 24 hours of the mites entering his skin, and an obvious erythema and perhaps wheal formation may be noted on the infested parts. The infestation may be aborted at this stage either because the parasite is removed by scratching, or because the mite, finding the reaction unfavourable, departs from her host. If parasites succeed in establishing themselves a second time on a host, their numbers never rise to the height recorded during the first infection

During the first few weeks of a first infestation, a patient is a silent carrier of the disease, but such carriers seldom transmit scabies.

Perhaps a few are immune to the antigen which it is believed the mite produces, and do not either become sensitized or suffer itch, others may be abnormally unaware of the subjective phenomenon known as itching and although heavily infested for several weeks make only few complaints of this symptom. Whatever the cause, it is possible for some heavily infested individuals to remain silent carriers of scabies and, in consequence, to disseminate the disease very readily. The value of regular health inspections in the prevention of the malady is therefore obvious

In some persons, itching may occur at the sites of some of the burrows, although the patient has been treated and is known to be cured; the assessment of post-scabietic pruritus may be difficult and entails the dissection of any residual lesions with a histological needle and examination of the lesions and their contents under a low-power microscope lens.

Treatment.—Many drugs, *e.g.* mercury, beta-naphthol, balsam of Peru, styrax, rotenone, etc., will cure the disease if properly applied.

Two methods of treatment are recommended :—

Benzyl benzoate.—Of many formulæ which have been suggested the following are of importance :—

1. Benzyl benzoate	33⅓	per cent.
Soft soap	33⅓	„
Spirit, mineralized, methylated . . .	33⅓	„
2. Benzyl benzoate	20–25	„
Spirit, mineralized, methylated	75–80	„
3. Benzyl benzoate	25	„
Lanette wax SX	2	„
Water	73	„

[illegible]

the burrows is no longer encouraged for it is needless and tends to spread secondary infection. On leaving the bath the patient dries himself and [illegible]

[illegible]

which the benzyl benzoate has been applied; therefore he should be [illegible]

[illegible]

on the following day, 24–36 hours later a shower or bath is given to remove the benzyl benzoate from the skin. The application of the emulsion or solution requires care and skill, it is of special importance to ensure treatment of all parts of the scrotum, perineum, perianal area, and feet. *The whole of the integument below the neck must receive treatment;* it is not enough to treat only those areas where lesions are visible. He should report to the medical officer once a week for six weeks *to ensure that he is cured. If it is found at the first medical* inspection (seven days after the treatment) that a patient is not cured, a second application of benzyl benzoate should be made. If the infection persists the patient should be referred to a specialist in dermatology.

Sulphur Ointment.—A preliminary bath, with soaping, is given; when *the patient has dried himself 2 ounces of ung. sulphuris are rubbed* thoroughly into the skin from the neck to the feet, twenty minutes being taken for this procedure. The routine should be repeated twice at intervals of twelve to twenty-four hours (*i.e.* three inunctions with sulphur ointment in all). The patient should be kept warm, as the therapeutic effect of the ointment is thereby increased, and in temperate climates it is best to keep him in bed.

Blonde persons, particularly those with red hair, develop sulphur der-

matitis easily, and for these it is advisable to dilute the ointment by adding 1 part of soft paraffin or zinc ointment to 2 parts of sulphur ointment.

General.—For patients with a low parasite-rate (*i e.* the majority of military cases), disinfestation of clothing and bedding is unnecessary, particularly if benzyl benzoate is used. If sulphur ointment is employed disinfestation of fomites is usually thought desirable. Fomites of all cases with a *high* parasite-rate must be disinfected.

Benzyl benzoate and—to a lesser degree—sulphur, are good for minor septic lesions such as pustules and infected excoriations. Therefore, in cases secondarily infected with pyogenic organisms it is usually advisable to deal with the scabies on the lines described above, and if any septic lesions remain they may be treated later by routine measures

If scabies is complicated by eczema, the patient should be referred to a dermatologist.

After receiving treatment for scabies, the patients should have a weekly skin inspection for a month Contacts of cases should be kept under observation, since early diagnosis and treatment will prevent the spread of infection

Prevention.—The importance of adequate ablution and bathing facilities cannot be over-emphasized, as also of satisfactory laundry arrangements for undergarments. The communal use of articles of clothing, such as sports clothing and the like, should be discouraged, whilst special care must be taken to ensure that blankets are marked in the usual way, in order to avoid the accidental transfer of one man's blanket to another

Contacts of cases should be kept under observation

A considerable aid in suppression amongst units is fearless reporting and the publication of incidence curves and tables

TICKS

These arachnids are usually divided into two families—Ixodidæ, hard ticks, and Argasidæ (more correctly, Argantidæ), soft ticks Some zoologists do not give familial rank to these groups and regard them as subfamilies only. Among ticks the Ixodidæ can easily be recognized by their terminal projecting mouth parts, and by the presence of a dorsal shield which is small in the female and in the male covers practically the whole body. The mouth parts of the Argasidæ are not terminal, consequently they are not seen in a dorsal view. There is no dorsal shield in either sex.

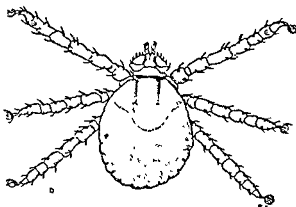
From the tick egg minute larvæ with only three pairs of legs emerge The larvæ of Ixodidæ (Fig. 6) await on grass, etc., the passing of a suitable host to which they attach themselves After gorging they drop to the ground, moult, and become nymphs These resemble the adult in having four pairs of legs but lack genital organs. Similarly the nymphs attach themselves to a host, and after dropping off, moult and become adults. Ticks requiring three individual hosts for their development are often known as three-host ticks. There are also two-host and one-host ticks

Though the Ixodidæ are of the utmost importance in veterinary medicine they are known to be responsible for only a few infections of man, such as Rocky Mountain spotted fever,* a typhus-like disease spread by *Der-*

* Another typhus-like disease occurring in India has been attributed to the bite of some tick, but the indictment remains to be established

macentor andersoni, and fièvre boutonneuse spread by *Rhipicephalus sanguineus*, the dog tick. These hard ticks may cause a form of acute ascending paralysis which, especially in children, may end fatally. It

Fig. 6.



Tick larva (After Castellani and Chalmers)

D. variabilis, the dog tick of North America, is the vector of spotted fever in the eastern United States This tick also transmits tularæmia.

Louping ill, an encephalomyelitis of sheep, common in certain parts of Scotland, is due to a virus said to be transmitted by a hard tick, *Ixodes ricinus*. Human infections, especially amongst shepherds, may occur.

When force is used in an attempt to remove an attached tick, one of two things happens—either the surrounding skin is unnecessarily torn, or, as is most probable, the body of the tick comes away leaving the mouth parts buried in the skin. This sets up severe irritation, and may even lead to septic infection, therefore, rather than forcible removal, the following course is advocated where time permits.

A small camel-hair brush should be dipped in turpentine, benzine,

that remains in the skin after a tick has been forcibly removed, cocaine should be applied to the spot and the rostrum extracted with needle forceps, and the wound treated antiseptically.

Against ticks, D.D.T. is of doubtful value, but clothing impregnated with dimethyl- or dibutyl-phthallate gives a fair degree of protection. When a tick-infested area has been located scrub clearance is desirable if it is practicable.

The Argasidæ in their feeding habits usually resemble bed-bugs rather than typical ticks. They hide during the day, and by night sally forth, and having fed return to their lairs again. The most important member of this family is *Ornithodorus moubata*, which is a host of the organism causing Central African relapsing fever. It is necessary to say a little regarding this vector.

Ornithodorus moubata

This blind tick (the eyeless tampan) is common throughout wide stretches of Africa including Uganda, Somaliland, and Nyasaland in the East, the Congo and Angola in the West, and the Transvaal in the South. It has also been reported in North-West Madagascar and to the South of Lake Chad. Its general appearance is well shown in Plate 2. It is a greenish-brown colour when alive, and, like all the Argasidæ, does not possess a shield or scutum, but is covered by a leathery integument This integument is dotted over with close-set granules and exhibits several grooves both on the dorsal and ventral surfaces. In gorged females these disappear. Important diagnostic characters are the broad rounded anterior extremity, the absence of a deep, waist-like constriction, the distinct tubercles on the distal segments of the legs, and the absence of eyes

Unfed adults are about 4/10ths of an inch in length, but a gorged female may be well over half an inch long and be very nearly of an equal breadth *O. moubata* lives in native huts and in rest-houses which natives may have occupied. It is commonest along trade, travel, and caravan routes. During the day it hides in cracks and crannies in the walls and floors, or about the bases of the vertical wooden roof supports, or in the thatched roofs, or more rarely in cracks in native wooden bedsteads. At night it sallies forth on the blood quest. It feeds both on man and animals, and engorgement takes from a few minutes to about two hours, according to the stage of the tick The bite may leave a tingling sensation behind it, but it is often painless and may pass unobserved. The fecundated female, after a meal of blood, lays from 50 to 100 nearly spherical, glistening, golden-yellow eggs in batches, the number in each batch varying The eggs, which are agglutinated into masses, are laid in the soil or in other hiding places They hatch in about twenty days, and as the hexapod larval stage is practically suppressed it is an eight-legged nymph which emerges from the egg-shell and the larval skin. Sometimes, however, the larvæ are free-living

There are three or four nymphal stages, and these, as well as the adults, may attack man. The adult may live for several years, and may exist for long periods unfed—in one instance, cited by Warburton, for so long as five years The offspring of an infected tick are themselves infective to at least the third generation

The bites are best treated by bathing the bitten part in very hot water and applying a strong solution of bicarbonate of soda If itchiness persists, smear with a menthol vaseline. For other points, including prophylaxis, *see* Relapsing Fever (p. 250).

O. savignyi, a closely allied species, has been proved capable of conveying relapsing fever, and is said to have been responsible for the spread

of the disease in Somaliland and Abyssinia. This tick differs from *O. moubata* in possessing two pairs of eyes, of which the posterior pair are the more easily seen. One of these lies on either side of the body in the space between the 2nd and 3rd pair of legs, and appears as a slightly raised, reddish dot. The beginner must beware of mistaking the much larger breathing spiracle for the eye. The hind tarsus of *O. savignyi* is longer than that of *O. moubata*, and for this reason the terminal tubercle in the former species appears very remote from the two preceding tubercles. This character will readily be appreciated if the hind tarsi of these two species are compared. For other tick vectors of spirochætes, *see* Relapsing Fever.

ANTS

As regards this group it need only be remarked that ants have been *incriminated experimentally in the spread of typhoid and cholera and* [illegible]

is present.

Ants have also been noticed to remove small fragments of infected scabs from the neighbourhood of smallpox patients and to store these at places a considerable distance off. It is possible that infection may occasionally be spread by this means.

Ants may be kept from food on tables by tying paraffin-soaked rags round the table legs.

If an infestation of ants occurs it is usually the larder that is raided. If the place of entry into the house can be traced, a small sponge soaked in sweetened water, placed near the entrance, will attract the ants and when the pores of the sponge are filled with them, it may be dropped in boiling water and the process repeated. To avoid the incursions of the [illegible]

Nests may also be destroyed by digging up the earth over and around them for several inches, pouring in about a pint of petrol or kerosene and setting it alight. Boiling water poured repeatedly into the nests is also useful. If the nest cannot be located, jam jars lightly coated inside with treacle may be placed at suitable points in the ants' runs. The worker ants are trapped in the jars in large numbers, and after a time the nest becomes so denuded that the queen ant either dies of starvation or moves [illegible]

(*see* Appendix I) is the method of choice, applied to the [illegible]

exterior surfaces of bamboo bashas, it will render these termite-proof for a long period.

COCKROACHES

To control these pests, floors should be swept and other feeding grounds kept as clear as possible of food debris. Residual spraying of kitchen walls and floors with 5 per cent. D.D.T. in kerosene (1 gallon for each 1,000 square feet of surface), repeated at fortnightly intervals, will effect a material reduction in numbers. Complete eradication is always difficult. Baits of poisoned food, such as sodium fluoride mixed with some soft food, may be of assistance. Breeding places should be tracked down and cracks filled in or liberally dusted with anti-louse powder (10 per cent D.D.T.). Drains are favourite resting-places and should always be investigated. Fumigation with sulphur dioxide and the like will deal fairly efficiently with nymphs and adults, but is unlikely to reach the eggs, which are protected by a specially hardened case. Care must be taken not to contaminate food with any poisons used.

WINGED PESTS

Under this heading Mosquitoes, Sandflies, Midges, House Flies, Stable Flies, Tsetse Flies, the Congo Floor-maggot Fly, Carcase Flies, and Hippobosca are included.

MOSQUITOES

Diseases transmitted by.—Malaria, dengue fever, yellow fever, filariasis, Rift Valley fever, tularæmia.

Mosquitoes constitute the family, Culicidæ, and are distinguished by the venation and scaling of the wing. The second, fourth, and fifth longitudinal veins are forked (Fig 7), and there are always scales on the hind margin of the wing. The Culicidæ are divided into two subfamilies . (1) Culicinæ, which have a very long proboscis, and scales on the longitudinal veins, and (2) Corethrinæ, which possess only a tiny proboscis, and have hairs on the longitudinal veins. These latter do not bite and are of no medical interest.

In the sub-family, Culicinæ, four tribes are generally recognized—Anophelini, Culicini, Megarhinini, and Sabethini. The first two include all the known disease carriers, and are considered hereafter. The Megarhinini are large non-biting mosquitoes with a proboscis recurved on itself like a pot-hook. The Sabethini are small jungle mosquitoes which may act as potential vectors of jungle yellow fever.

ANOPHELINI

This tribe may be regarded as comprising one genus only, *Anopheles*, which includes all the known carriers of malaria. The sex of anophelines, and of the vast majority of culicines, may be recognized by the densely haired and plume-like antennæ of the male, those of the female being very sparsely haired (Fig 7). Female *Anopheles* may be identified by their palpi which are as long, or almost as long, as the proboscis, whereas those of female culicines are always distinctly shorter than the proboscis,

Fig 11.—Culicini—*Culex fatigans.*

a Male *b* Female

Fig. 12 —Culicini.

a Egg raft (side view), *b* Larva (note resting position, body hanging at an angle from surface), *c* Pupa *d* Empty puparium from which mosquito has emerged

Yellow Fever —*Aedes ægypti* has long been regarded as the sole vector of yellow fever While this remains true for the classical urban yellow fever, recently other mosquito vectors (*Aedes leucocelænus* , *Hæmagogus capricorni*, etc.) have been proved capable of transmitting that variety of the disease known as jungle yellow fever, which is endemic over widespread areas in South America where *Aedes ægypti* does not exist. (*See* p. 332.)

In order to distinguish *A. ægypti* (Fig 13) from other black and silver mosquitoes, two characters, taken in conjunction, will suffice. These are the absence of any narrow curved scales on the back of the head and the vertex, and the arrangement of the "lyre" marking on the dorsum of the thorax. To determine the first of these, a microscope is necessary Failing this, the following characters can be noted with a hand lens, or by the unaided eye : the unbanded proboscis, the "lyre" on the thorax, the silver scutellum; the cross bands on the abdomen , and the leg markings—tibiæ entirely dark, hind tarsi with five bands, tarsi of other legs with two bands.

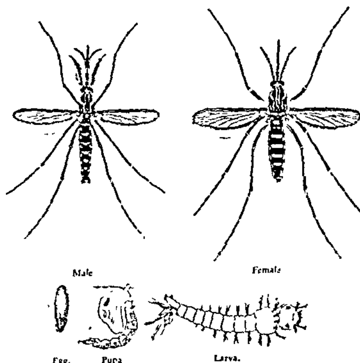
Dengue.—*Aedes ægypti* and *Aedes scutellaris* are proved transmitting agents of the virus of dengue. Two other mosquitoes are under grave suspicion, *Aedes albopictus* and *Armigeres obturbans*. *A. albopictus*, a much commoner mosquito than *A. ægypti*, is distinguished from it by the single broad longitudinal stripe replacing the lyre on the thorax. *Armigeres obturbans* is a large black mosquito with no silver markings visible in a dorsal view, but the under surface of the abdomen is silver with a transverse black band on each segment. The proboscis in both sexes is bent, with the convexity dorsal.

Filariasis.—Complete development of the larva of *Wuchereria bancrofti* has been observed in a large variety of anopheline and culicine mosquitoes.

Among the most common transmitters are: *Culex fatigans*, *C. pipiens*, *Aedes variegatus* (*Stegomyia scutellaris*), *Anopheles gambiæ* (*A. costalis*), *A rossi* (*A. subpictus*).

The sandfly *Phlebotomus sergenti* var *mongolensis*, has also been incriminated as an experimental host.

Fig 13.—Culicini—*Aedes ægypti* = *Stegomyia fasciata*. The "Yellow Fever Mosquito".



Rift Valley Fever.—This somewhat localized disease occurs as a fatal epizootic amongst ewes, lambs, and cattle. It is transmitted to man in Kenya, Uganda, the Southern Sudan, and some parts of French Sudan

and French Equatorial Africa, where it causes a non-fatal dengue-like illness. Available evidence suggests that mosquitoes of the genus *Mansonia* may be vectors.

CONTROL OF MOSQUITOES

Experience during the war (1939–45) and the development of D.D.T. have combined to bring about radical changes in our tactics for the control of mosquitoes, both as regards the means employed and the emphasis on the different available methods. The present military approach to control of mosquitoes is briefly summarized as follows:—

1. *Camp siting.*—Of great importance if a choice is possible.
2. *Personal protection.*—Of fundamental importance because it can always be practised, the appropriate measures depending on the tactical conditions. The measures employed are: protective clothing, repellants, mosquito nets, and, where possible, screened quarters.
3. *Residual spraying.*—Residual spraying of quarters with D.D.T. ensures that a mosquito which alights on the sprayed surface is killed after a short time.
4. *Insecticide sprays and aerosols.*—These agents produce a rapid "knock-down" of adult mosquitoes; their lethal effect is enhanced by a combination of pyrethrum and D.D.T. They are used in quarters to supplement residual spraying, but their greatest application is perhaps in fox-holes, slit-trenches, dug-outs, and so forth.
5. *Larval control.*—Measures to control mosquito larvæ may be either temporary or permanent according to the length of time the area is to be occupied. A stay of only a few months calls for temporary measures, permanent measures may require several years to complete. If a site is not to be occupied for longer than a week or so, anti-larval measures will not have time to yield useful dividends.

Each of these measures will now be considered in turn.

Camp siting.—When active operations are in progress, tactical requirements take precedence over all else; but in the absence of active operations a camp should never be sited until someone has been consulted who can speak with authority both about the malaria season and the distribution and habits of the disease-carrying mosquitoes of the locality. It is often impossible to select a camping area free from all risks and the choice may fall not on the site where risk is lowest but on that where effective control is most easily attainable with the means at hand.

Personal protection.—Effective personal protection is of the highest [illegible]

tective clothing, repellants, and nets, with screening of quarters, when this is feasible, as an additional safeguard.

Protective clothing.—The material is light gabardine and this is proof against mosquitoes. The suit must have long trousers and long sleeves with insect-proof gussets in the cuffs. This clothing must be put on at

least half-an-hour before dusk and it may have to be worn throughout the day in some areas It is important to protect the ankles by wearing mosquito boots or boots and puttees.

Repellants.—Earlier repellants, to which various objections were raised, have now been replaced by a mixture of synthetic substances of the following composition: Indalone, 20 parts; Rutger's 612, 20 parts; Dimethyl phthallate, 60 parts. The issue is two ounces a week for each man. The mixture is used because several species of mosquito are not repelled by each one of the three ingredients; during a shortage of the other two constituents, dimethyl phthallate alone gave good results against the important disease-vectors.

During the hours of darkness men apply repellant to the exposed skin of the face, neck, wrists, and hands, but it should be kept out of the eyes. Application must be repeated two-hourly as long as the man is up and about.

In forward areas where mosquito nets cannot be used, repellant fluid is employed to impregnate head-veils, oversleeves, and oversocks. These protective garments are made of fine string "fish-netting", their function is not to exclude mosquitoes by mechanical means but to act as a vehicle for the repellant. Their mesh is wide enough not to interfere with vision or comfort and men willingly use them, especially as protection during sleep. The only stipulation about mesh is that the strands must not be so far apart that a mosquito can alight without touching a strand with one of her legs. The impregnated netting is carried in a waterproof wallet *with a cloth lining and re-impregnation is done by soaking this* cloth lining once a week with half-an-ounce of repellant lotion.

Mosquito nets.—Mosquito nets are used to give protection during sleep and their proper use is of the greatest importance for it is during sleep that a man is most liable to be bitten by mosquitoes. The net itself must be carefully maintained and inspected daily to ensure that it is free from tears or holes that would admit entry of mosquitoes. Nets must be properly tucked in under mattresses and arranged by whatever means [illegible]

purchase nets from local shops or traders it is important to ensure that the nets are of the right mesh to exclude mosquitoes. The mesh of cotton [illegible] of [illegible] ole [illegible] ice.

(Fig. 14)

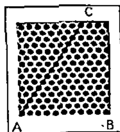
The mesh of the nets issued to the Army is 28/29 holes to the square inch

Cotton thread is standardized by weight, being described as "30", "40", "50", etc., the higher numbers indicating the thinner thread. The thread used for army nets is 30/40 cotton (*i.e.* 30 warp, 40 bobbin).

Screened quarters.—Screening of quarters is becoming a much com-

moner feature of buildings in the tropics but it is not wise to regard such screening as conferring absolute protection; therefore mosquito nets, repellants, and protective clothing are not to be neglected because quarters

Fig. 14.



Shows the correct method of counting the mesh of cotton netting The mesh of this net is the sum of the counts made along the lines AB and AC, the hole at A being counted twice

are screened. Properly protected quarters with double doors are very welcome additions to life in the tropics—they keep out other pests as well as mosquitoes But it is important to see that the wire screening is kept in good repair—otherwise the building may become a mosquito-trap and a source of danger rather than protection to its occupants.

Care is necessary that wire gauze is of the correct mesh to exclude mosquitoes The mesh is calculated by counting the number of holes to the linear inch. The size of the openings varies with the count to the inch and also with the thickness of wire used, the latter being expressed in terms of Imperial Standard Wire Guage. To exclude mosquitoes from buildings, 14 mesh screencloth of 30 I S.W.G. will suffice in most districts, but when certain small species prevail a 16 mesh of 28 I S W.G. is necessary In the former case the wire is 0 0124 inch in diameter and the apertures measure 0 059 inch

Residual spraying.—Spraying of D D T. in such a manner as to ensure a residual action is one of the most effective means of directly reducing the number of adult mosquitoes and indirectly the number of larvæ (*see* Appendix I) D D T residual spraying may be used both indoors and out of doors The dosage recommended for indoor spraying is 50–100 mg a square foot (1–2 quarts of 5 per cent. solution in kerosene for each 1,000 square feet) This should be repeated every two months Bigger doses have been tried with the aim of prolonging the residual effect but the dosage recommended has been proved the best in many trials

An important point is that huts in nearby native villages should first receive attention—for it is in these dwellings that the highest number of infected mosquitoes will be killed After the native quarters and adjacent villages have been sprayed, attention should be given to the European-occupied part of the camp.

Outdoor spraying is necessary to deal with mosquitoes of the "enter, bite, and leave" variety—*An. maculatus*, for example—which do not rest

indoors and will not, therefore, come in contact with D.D.T. sprayed on inside walls or furniture.

Outside, area spraying is carried out with 5–10 gallons of 5 per cent. D.D.T. an acre. The spray is applied to all vegetation and to exteriors of all buildings within a camp area and for a radius of 50 yards beyond. This method is useful because mosquitoes, although they may cover longer distances than we had once thought, usually progress in a series of short flights, and are thus likely to come to rest at some point within the sprayed area.

Barrier spraying may be used to give temporary protection within a limited area of special importance—for example, a bridgehead may be protected by spraying a belt of 100 yards wide all around the area of importance. Within the area itself, mosquitoes are controlled by insecticidal sprays. *Weekly applications are required for full control.*

Insecticidal sprays and aerosols.—The principle underlying the various mixtures employed is that mosquitoes are stimulated into flight and thereby brought into contact with a dose of insecticide which quickly knocks them down and kills them. *In forward areas where residual* [illegible]

[illegible]

gun, or, more efficiently, by the use of individual sprayers (sparklets). An individual sprayer is enough for 1,000 cubic feet; in a flit-gun the dosage is 10 c.cm. for each 1,000 cubic feet.

The aerosol bomb is also used. Four seconds' spraying is needed for each 1,000 cubic feet. The bomb has a total capacity of 16 ounces and will give 15 minutes' continuous spray, which is equal to 1 gallon of official test insecticide (*see* Appendix I). A single bomb will clear mosquitoes from one acre of jungle under favourable conditions of weather. [illegible]

[illegible]

Larval control.—Control of larval breeding-places is the last of the measures to be undertaken by a military unit in a malarious area, and it is useful only if the site is to be occupied more than a month or so. [illegible]

[illegible]

are either temporary or permanent. Certain points of camp discipline, [illegible]

[illegible]

mosquitoes may breed, especially *Aedes ægypti*, the most important vector of yellow fever and dengue fever.

Details of temporary and permanent anti-larval measures are given in

two official army manuals which should be consulted, *Army Manual of Hygiene and Sanitation* and *The Use of D.D.T. in the Field*. Only an outline is given here.

Temporary measures.—Malariol or some similar preparation can be used to treat collections of standing water at weekly intervals, the dosage being 15–20 gallons an acre. Solutions or emulsions of D.D.T. can be used for the same purpose, either 1 quart of 5 per cent. solution or 5 quarts of 1 per cent. solution an acre, depending on the apparatus available for its distribution. Paris green (copper aceto-arsenite) is widely used as a larvicide, especially for anophelines, in an amount of one pound an acre. The chemical is used as a 2–5 per cent. mixture with some inert light dust (road dust will serve), it must contain 55 per cent. arsenious oxide and be fine enough to pass through wire gauze of 30 meshes to the linear inch.

Permanent measures.—Before undertaking permanent anti-larval measures the first need is to determine the local vectors and become fully informed of their habits—whether they prefer light or shade, where they actually breed, and so forth. Sanitation cannot be successful if the measures are adopted in haphazard fashion, intelligent planning is necessary in the light of all that can be learned of local conditions and mosquitoes, in other words, it is necessary to practise "species sanitation". An important general principle is to avoid any measures for the destruction of one species if the same measures are likely to encourage the breeding of another—perhaps a more dangerous vector.

According to local conditions various measures may be adopted: bush clearing, filling, drainage, alteration of salinity of water, stream-training and "lido" formation, and the use of biological methods by introduction into ponds of fish, such as *Gambusia*, that eat larvæ. Often it is more important to clear vegetation so that fish already present can get at the larvæ than to introduce new species of fish. By itself, this measure is often disappointing.

NOTE.—The insects most likely to be mistaken for mosquitoes are the harmless midges belonging to the Chironomidæ. These, however, nearly always have the long, narrow abdomen turned up at the end. They do not possess a biting proboscis, and the wing venation differs widely.

Biting Chironomidæ are sometimes confused with mosquitoes, but a glance at their wings dispels the illusion. The intermediate hosts of *Acanthocheilonema** *perstans* have been shown to be *Culicoides austeni* and *C. grahami*, the larval development taking seven or eight days. The females, which alone attack man, will bite by day as well as by night.

SIMULIIDÆ

In some parts of the world these are known as blackflies.

Diseases transmitted by.—The filarial worm, *Onchocerca volvulus* is transmitted by *Simulium damnosum* in which the larvæ take eight to ten days to reach the infective stage. A closely allied helminth, *O. cæcutiens*, is believed to be transmitted by *S. avidum*, *S. mooseri*, *S. ochraceum*.

The bites of *Simulium* are particularly severe and painful when they

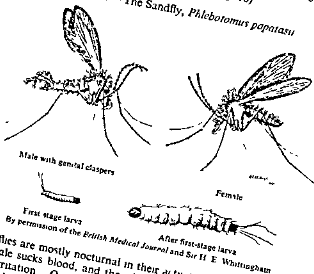
* *Dipetalonema*.

sandfly-fever patient in the first day of his illness   The virus is tra
mitted to the progeny of the infected female sandfly

PHLEBOTOMUS

Small flies having the wings and body very thickly covered with hair The wings are held at an angle of about 45 degrees from the body and th large black eyes are a prominent feature (Fig 16)

Fig 16 — The Sandfly, *Phlebotomus papatasii*



By permission of the *British Medical Journal* and Sir H E Whittingham

Sandflies are mostly nocturnal in their activities   In most species only the female sucks blood, and though the flies are minute the bite causes severe irritation   On the slightest disturbance the insect moves by short rapid flights with sudden changes of direction to left or right, suggesting to some extent the movements of a flea

Its small size enables it to creep through the mesh of ordinary mosquito nets   Because of its weak flight and small size it may readily become entangled in the hairs of the forearm

Reproduction —Atmospheric conditions optimum for breeding are a temperature of 80° F and a high relative humidity   Breeding ceases below 60° F

Eggs are laid in dark damp cellars, dug-outs, caves, cracks, and fissures in the soil, and under damp stone walls   Slightly moist crevices in the banks of nullahs, drains, or the like, if well above water level, are favourite spots for egg laying

Larvæ hatch out from the eggs in about nine to 12 days   For their growth, moist organic matter is essential, as well as shelter and darkness, but too much moisture will drown them   If soil or other material adheres to the fingers and does not fall off when rubbed gently between them, it may be taken as certain that it comes from a place too damp for sandfly breeding   The larvæ are minute and caterpillar-like, according

to the stage of development, the body has either one or two pairs of large bristles at the posterior end. The larval stage lasts 23 to 30 days. When fully grown the larva pupates and the perfect insect emerges from the pupa about seven to ten days later. In all, therefore, reproduction takes about 40 to 52 days. In nature the stages of development are not easily found. They have been studied mostly under laboratory conditions, and even then under technical difficulties. Exactly the right amount of moisture is required for the larvæ, which on the one hand are extremely sensitive to dehydration, and on the other are easily drowned by excess of water in the medium.

Examination for Immature Forms.—Large quantities of suspected soil or mud have to be examined in searching for the larval stage, and this is a time-consuming and often fruitless task, even in the immediate neighbourhood of quarters where there is an epidemic of an undoubtedly sandfly-borne disease.

The suspected material is filtered through sieves with mesh of decreasing size down to 40 strands to the linear inch, and finally through muslin, from which the larvæ can be floated on to the surface of a saturated solution of sugar in water where they can be seen with the aid of a hand lens

[illegible]

Preventive Measures

1. Elimination of all breeding places within 250 yards will greatly reduce the nu[illegible] because the range of flight is sc[illegible]ss, and organic matt[illegible] to be dealt with. [illegible]

(*a*) Removal of all rubbish, especially heaps of rubble.

(*b*) Levelling the ground by rolling, and, in special cases, by rendering the surface impermeable with cement, asphalt, tar, or similar material Covering a fissured area with sand and rolling it is also effective.

(*c*) Facing and pointing of walls of buildings in which crevices have appeared that are likely to form breeding places for the insects.

(*d*) Eradication of cracks and crevices in banks of streams, drains, etc., by smoothing off the surface or lining with cement or concrete.

2. Keeping rooms and barrack-rooms clear of cobwebs and rubbish where sandflies may hide during the day.

3 It is important to ensure good lighting and adequate ventilation with consequent air movement; this the sandfly dislikes because it causes difficulty in flying Installation of fans is useful for the same reason.

4. Sleeping under a sandfly net with a mesh of 45 to the square inch is not worth the discomfort. This affords only uncertain protection, a D.D.T.-impregnated mosquito net is more useful.

5. If possible sleeping quarters should not be on the ground floor but

on the first floor or higher. Sandflies are much less numerous in roor above the ground floor.

7. Repellants are important under active service conditions. Dimeth phthallate is highly effective.

Sandfly Destruction

1. D D.T. residual spray (*see* Appendix I) with a 5 per cent. solution as for mosquitoes gives almost 100 per cent control.

2. Spraying of mosquito nets with D.D.T. is a valuable additional measure.

3. Outdoor spraying with D.D T should include all likely resting places, including bridges and culverts.

HOUSE FLIES

Diseases transmitted by.—The common house fly (*Musca domestica*) is definitely known to contaminate food by conveying pathogenic organisms on its body, wings, legs, and foot-pads (Fig 17) or depositing them in its regurgitations or its droppings. The last mentioned is the method which has been proved to occur in amœbic dysentery. Because it feeds indiscriminately on human excreta and food the fly is an extremely efficient vector of excremental disease—in warm countries probably the chief factor affecting their incidence. Septic skin-lesions, ophthalmia, and most diarrhœal diseases are among the host of maladies that may be caused or aggravated by flies in tropical and subtropical countries. The lesser house fly (*Fannia canicularis*) and the latrine fly (*F. scalaris*) have the same filthy and dangerous habits as *Musca domestica*.

Fig 17 —*Musca domestica.*



Foot, showing hairs on which bacteria, etc , lodge

In India, *M. vicina*, *M humilis*, and *M. sorbens* (=*nebulo*) are common, these, with *M domestica*, are the house-, bazaar-, and camp-frequenting species; in their feeding they are omnivorous Other flies which are o less importance as disease carriers, are the grey flesh-fly (*Sarcophaga*), which breeds in offal, and the "Bluebottle" (*Calliphora*) and "Greenbottle" (*Lucilia*), both of which breed in flesh of all kinds

In hot countries flies are most numerous where vegetation is scanty, where it is abundant flies are reduced in numbers because other insects

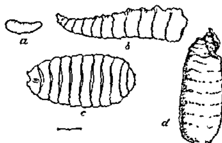
destroy their eggs. Since flies breed in rotting organic matter, filthy conditions and poor sanitation obviously favour large fly populations.

The commonest of the English flies is *M. domestica* and it is necessary to know something of its life history in order to understand the means used for its prevention and destruction.

Musca domestica

The female lays eggs in batches of 120 or so, and she lays four batches during the year. These are deposited in rotting organic and vegetable matter of all kinds—human excreta, animal or vegetable manure, food,

Fig. 18.—Musca domestica.



a Egg *b* Larva *c* Pupa *d*. Empty puparium

or offal. The eggs are small, white, sticky, and rather elongated; they can be seen with the naked eye. (Fig. 18, *a*.) They hatch in two to four days, depending on the temperature. The larva (Fig. 18, *b*) is cream coloured and tapers to one end; it is very active and burrows quickly beneath the surface, shunning the light. It feeds on the rotting matter in which it lives and becomes fully grown in about five days, gradually
When mature it borrows into the surrounding earth
ens and darkens still further
s formed. The pupal stage
dually becoming very dark
merges from the end of the
pupal case and pushes up to the surface. In loose sand flies have actually been known to reach the surface from a depth of 10 feet. The wings expand and dry, and the young fly runs briskly around for the first few hours of its life before it is able to fly—the "crawler" stage.

The breeding time of the fly varies greatly with the temperature; usually it requires from 10 to 14 days. The most favourable temperature is between 18° to 24° C.; as the temperature rises above 24° C., the fly population diminishes proportionately.

Prevention and Destruction of Flies.—The general lines of procedure may be summarized as follows:—

1. *Removal of breeding places*—For example, by sanitation. Fly-proofing of latrines denies entry to or exit from a potential breeding place.

2 *Treatment of breeding places that cannot be removed*—With D.D.T. for ordinary breeding places, and D.D T. in orthodichlorbenzene for carcases or corpses
3. *Residual spraying with D D T.*—Indoor spraying of all buildings if flies are numerous and of selected buildings if flies are less numerous.
4. *Use of swats and traps*—These are simple measures of obvious value. Traps may be of the bait, poisoned, or tanglefoot varieties.
5 *Protection of food.*—This is done by fly-proofing of cookhouses, dining-rooms, cupboards, latrines, and so forth. It is the last line of defence but of vital importance.

Fig. 19—*Musca domestica.*



Just emerged from the pupal case Note the wings, as yet unexpanded, folded and crumpled on the back of the insect

Removal of breeding places.—Fortunately, fly eggs form the food of many other creatures, and the fly population is reduced to some extent by their activities and other natural events.

If all waste, manure, excreta, offal, swill, and organic refuse is properly disposed of there will be no breeding within the area under control, but in practice it is rarely possible to abolish all places for fly-breeding, and

Fig 20.—*Musca domestica*



The common house fly

outside actual camp areas, fly-breeding cannot possibly be prevented altogether; therefore, destructive measures against adult flies must be used on a wide scale. Control of breeding-places is the fundamental step, other measures serve to stop inevitable leaks that this measure by itself cannot avoid

Treatment of breeding-places that cannot be removed.—Against adult flies, D.D.T. has a powerful lethal action but no repellant effect; *it does* [illegible]

The object, therefore, is to cover the surface of a breeding-area with a residual film of D.D.T. in sufficient amount to kill flies alighting on the surface or emerging from pupæ. The dose required for this is 100 mg. of D.D T. for each square foot of the surface—that is, 8 ounces of 5 per cent. D.D.T. in kerosene for each 100 square feet. Manure heaps, garbage dumps, refuse pits, and the contents of latrine trenches are covered with a uniform spray by hand-guns or knapsack sprayers—according to size of the area. As well as the breeding-place itself, the ground for 6 feet all round the actual breeding-material should be treated. This method is not of value for treatment of breeding-places to which fresh material is constantly being added, or for an area in which new [illegible]

has been suggested.

Residual spraying with D.D.T. (*see* Appendix I).—If there are great numbers of flies and many breeding places, all surfaces of all rooms, *huts, tents, or other buildings, must be treated in the ordinary way. The* effect of this indoor spraying will not be apparent for three or four days after treatment, thereafter good results become more and more apparent.

Selective spraying with D D.T. is advisable if flies are not so numerous [illegible]

butchers' shops, slaughter-houses, and dining-rooms. Two quarts of 5 per cent. solution or emulsion for each 1,000 square feet should be used. [illegible] corners of walls [illegible]

incinerators, latrine seats and screens, stables, byres, pigsties, and so forth.

Where residual spraying has been done insecticidal sprays of pyrethrum with D.D.T. are not required. They are highly effective against flies as well as mosquitoes, but they should be conserved for use against mos*quitoes in forward* areas and other places where residual spraying is not feasible

Use of swats and traps.—The simple but effective fly-swat should not be neglected.

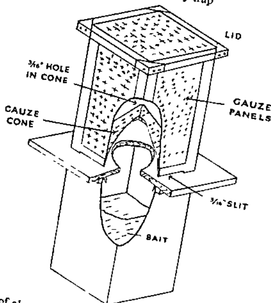
Traps of three kinds are now in use—baited (Bruton trap), poison

'Sodium arsenite trap), and the tanglefoot trap. Traps are useful but, with the arrival of D.D.T., subsidiary means for controlling flies.

The Army box-trap (Bruton trap).—The fly is attracted to the trap by a bait which is moist, rotten, and high-smelling and therefore attractive to flies. The traps should be placed away from cookhouses and living-quarters as they draw flies towards them; the ideal site is between the camp and any nearby village—usually the main source of flies.

The trap (Fig. 21) consists of a fly-wire cage in which the flies are trapped; this is set up on a board with a large hole in the centre, with a

Fig. 21.—Box Fly-trap

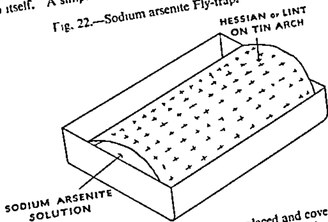


small aperture of about three-sixteenths-of-an-inch between the cage and the board. The board is placed on a tin containing a large mass of rotting swill or offal which should be kept moist to ensure continued putrefaction which is necessary to keep the bait attractive to flies. The flies enter between the trap cage and the base board, they pass into the bait-tin, feed, and fly up towards the bright light, the trap being so placed in the open that the light will shine into the bait tin. This brings the flies into the trap through a small hole in the top of a fly-wire cone and they die rapidly in the trap, which should be emptied periodically by removing the top and burning the flies. New bait should be placed in the trap every seven or ten days and the discarded bait should be burned.

The smell of these traps will deviate flies from the camp buildings; properly sited, they will destroy large numbers of flies.

The Sodium arsenite trap.—Sodium arsenite (1–2 per cent.) dissolved with 10 per cent. sugar in water makes a very effective poison trap. The flies take about two or three minutes to die; therefore, they seldom die in the trap itself. A simple form of this trap is illustrated in Fig. 22. It

Fig. 22.—Sodium arsenite Fly-trap.



is made from a tin tray in which an arch of tin is placed and covered with hessian or lint. This is kept moistened with the solution of sodium arsenite in the tray by capillary action. These traps are very effective in dry weather when moisture is what the flies most need. The traps should be set in places where flies are likely to be numerous—near latrines, for example, they should be used on a large scale, but sodium arsenite is poisonous to man and care is necessary to avoid accidents.

The tanglefoot trap.—Resin (5 parts) in castor oil (8 parts) is smeared on paper (fly-papers), wires, or strips of tin, and these are put in suitable places. Unfortunately tanglefoot is not very satisfactory in dry dusty climates because dust quickly destroys its adhesive properties.

Protection of food.—The final defence against fly-borne diseases is the protection of food by fly-proofing. Food should be protected at all stages; if possible it should always be transported in fly-proofed containers and stored, prepared, and eaten in fly-proofed rooms.

Food liable to contamination by flies should always be kept covered up and preferably in a fly-proofed safe. Eating- and cooking-utensils shoul also be carefully protected.

Protection of food is the most important single means of guardin against fly-borne diseases because we cannot control breeding-plac outside the camp-areas and we cannot destroy all the flies that come from the surrounding villages, which are usually the most dangero breeding-places, for there filth, flies, and carriers of disease, are togeth

Buildings are most effectively fly-proofed by covering the windows w fly-wire, and by making self-closing doors of fly-wire on light woo frames. If fly-wire is not available old mosquito- or sandfly-nettin satisfactory, though less durable. Doorways can be covered with netting hung loosely as a curtain that moves gently in the wind; a

bead curtain may be improvised from strings with "crown corks" tied on to them

Another important measure is to keep all latrines fly-proofed so that flies are denied all access to pathogenic organisms inside the camp, this is particularly important in countries where flies are prevalent and dysentery and diarrhœa are common.

THE LESSER HOUSE FLY (*Fannia canicularis*) (Fig 23)

This fly belongs to the Anthomyidæ, and in common with other members of this family the distal portion of the fourth longitudinal vein of



Fig 23.—*Fannia canicularis*



Fig 24.—*Fannia canicularis*. Larva

the wing does not bend forwards towards the third vein (Fig. 25) It must be emphasized, however, that neither *M domestica* nor *F. canicularis* can be identified by their wings alone, for many other flies have exactly the same arrangement of the veins. A useful diagnostic character shown by *F. canicularis* males is a yellowish, translucent patch on either side of the base of the abdomen The vast majority of flies found in houses in England during the early summer belong to this species.

It usually breeds in old vegetables or vegetable refuse, but a favourite breeding ground is human fæces The larva is a peculiar dirty-white coloured creature, possessing tassel-like processes from each segment of the body, shown well in the accompanying illustration (Fig 24). The other stages and details of development resemble those of *Musca domestica*.

Since the larvæ of the fly often live in vegetables they sometimes find their way alive into the human intestine, thus causing a form of intestinal myiasis.

Preventive and Destructive Measures.—As for *Musca domestica*, except that the favourite breeding place of this fly must receive special attention.

THE STABLE FLY (*Stomoxys calcitrans*) (Fig. 26)

As will be seen, this fly is rather like the house fly, but it has a spotted abdomen and is a blood sucker, being furnished with a stout proboscis The inclination of the distal portion of the 4th longitudinal wing vein is intermediate between that of *Musca* and *Fannia*. (Fig 26, *a*)

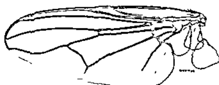
It commonly attacks animals, biting mules and horses about the fetlocks, and drawing scarlet beads at every thrust It also bites humans, usually through thin clothing, and it has been said to carry the virus of

Fig 25.—Wings of Calypterate Flies.

NOTE —These species cannot be identified by their wings alone



Fannia canicularis (Linnaeus 176[illegible])



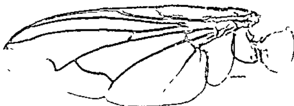
Stomoxys calcitrans (Linnaeus 1758)



Musca domestica Linnaeus 1758



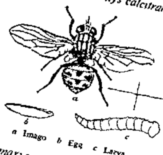
[illegible] pol[illegible] (Robineau Desvoidy [illegible])



Calliphora erythrocephala (Meigen, 1826)

poliomyelitis. *Stomoxys* probably acts as the mechanical vector of many important diseases, notably surra, an important veterinary disease due to *Trypanosoma evansi*.

Fig. 26.—*Stomoxys calcitrans*



a Imago *b* Egg *c* Larva

Many species of *Stomoxys* occur throughout the world *S calcitrans* is the only one found in Europe Dimethylphthallate is an efficient repellant.

TSETSE FLIES

The tsetse flies, *Glossina*, constitute a genus of the family Muscidæ, and are found only in Africa and Arabia. They are brownish flies and are distinguished by certain peculiarities in the wing venation. The course of the fourth longitudinal vein is characteristic of *Glossina*. It curv strongly forward to join the obliquely placed anterior cross-vein, an bending forward again at its junction with the posterior cross-vein, touches the margin of the wing at a point much anterior to the tip. Th cell lying between the proximal portion of the fourth and fifth veins has some resemblance to a butcher's cleaver. Reference to Fig 25 and Plate 3 will illustrate this characteristic appearance. The fly deposits at a birth a single mature larva (Plate 5) in a carefully selected spot. A favourite site is under trunks of fallen trees, and a light soil with some degree of shade is essential. Immediately after birth the larva buries itself and pupates. The duration of this stage varies, but it is often from three to four weeks, the time depending largely on the temperature. The pupa case is ovoid and easily recognizable by the two posterior protuberances (Plate 6).

There are about twenty species of *Glossina*, and of these *G. palpalis*, *G morsitans*, *G. tachinoides*, *G. brevipalpis* and *G. swynnertoni* have either been infected with "human" trypanosomes, or otherwise implicated in the spread of sleeping sickness. *G. palpalis* (Plate 4) and *G. morsitans* (Plate 3) are the most notorious species The banks of lakes and rivers overhung by trees and scrub form the favourite abode of *G palpalis*. Its natural range from water rarely exceeds thirty yards, though it may follow victims considerably farther. *G. morsitans* is much less restricted in its haunts than *G. palpalis* and inhabits as a rule moderately wooded country, and is not dependent on the propinquity of water. It does not occur

continuously throughout suitable country, but tends to be restricted to limited belts.

As is well known, tsetse flies are attracted by rapidly moving objects like motor-bicycles and motor-cars. They have a quick darting flight, so that the tsetse seems to "come out of nowhere", so suddenly and, as a rule, silently does it arrive, and so lightly does it settle on its victim.

Prophylaxis.—*Breeding places may be dealt with by the clearance of* jungle, scrub, etc., for a distance of thirty yards from the banks of lakes, rivers, or streams.

ployed for the purpose and are sent out into the jungle each night. Many hundreds of flies may be caught in this way.

Glossina species are susceptible to D.D.T. Thus 200 mg. of D.D.T. for each square foot of cloth will kill in two to four hours all insects of the species *G. tachinoides* that have had three or more minutes' contact with the impregnated cloth. *G. palpalis* is rather less susceptible but application of 5 per cent. D.D.T. emulsion as a spray or paint to the hides of domestic animals may be a useful means of controlling tsetse flies in sleeping sickness belts.

Harris's trap is of value. It consists of a framework of light wood covered by Hessian cloth and is roughly triangular in section with a flat uncovered top. The latter is 6 feet long by 3 feet wide, the sides converging below to about 3 inches apart with a narrow open slit along the bottom. The trap is hung so that the open slit is 48 inches from the

of pedestrians or cyclists, or on the hoods of motor cars, and may be carried for miles in this way. On this account restriction of vehicles to fixed

Horses should be similarly protected.

THE CONGO FLOOR-MAGGOT FLY

This fly, Auchmeromyia luteola, is chiefly of importance in that it is the parent of the well-known Congo floor-maggot, the only dipterous larva known to suck human blood. Although first discovered in the Belgian Congo, the maggot is not well named for it is widely distributed in tropical and *sub-tropical Africa. It is said* that its distribution coincides with that of the Negro and Bantu races and that it does not occur in countries inhabited by Arabs and Berbers.

It was frequently found in the East African war area and is of some

interest, as, owing to its peculiar habits, its presence causes natives to vacate huts which harbour it.

sexes and the second abdominal segment in the female is twice the length of the same segment in the male, which is not the case in *Cordylobia*. *A luteola* has also a narrower and more elongated body than *C. anthropophaga*.

A. luteola ...

... native huts which the female fly haunts or in their neighbourhood.

The Larva.—It hatches from the ...

... comparatively large quantities ... but, if numerous, may ... of blood from their sleeping victim

Prophylaxis.—General cleanliness and the enforcement of sanitary measures. The use of high beds. Sleeping mats and blankets should be searched for eggs and larvæ as it is possible the latter may be transported in such impedimenta. Infected huts can be rendered habitable by firing the ground or by digging up floors and removing the surface soil, which can then be disinfected.

CORDYLOBIA ANTHROPOPHAGA (TUMBU FLY)

See Myiasis (p. 203).

CARCASE FLIES

Under this term several genera are considered, including the "Bluebottles" (*Cynomyia*, *Calliphora*, etc.), the "Greenbottles" (*Chrysomyia*, *Lucilia*, etc.) and *Sarcophaga*—the hairy, grey-coloured flies found on decomposing material.

Diseases transmitted by.—It is more than probable that the "Bluebottles" and "Greenbottles" convey bacteria and protozoa to foodstuffs. Such flies were responsible for the cases of external myiasis (wound infection) commonly met with in France and elsewhere during the war of 1914–18. But such infestations were not without compensation, for the larvæ removed dead and damaged tissues.

"BLUEBOTTLES"

This term includes the common *Calliphora*, large flies with a dull thorax and an abdomen of a deep blue metallic lustre. They are the largest of the brightly burnished flies, and, in addition, the cheeks are very hairy.

"GREENBOTTLES"

This term includes several genera, and is applied to flies whose bodies show a very bright lustre, ranging in shade from a vivid blue-green to a green-bronze, and they are not so hairy as the former flies.

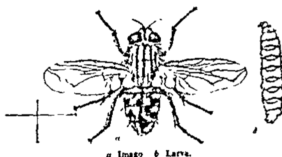
these are large and stout.

It has been shown that the species, *L. sericata*, which was at one time popular as a "surgical maggot" in view of its saprophagous properties, will attack and invade healthy living tissues.

SARCOPHAGA

The life-history of these insects corresponds in most details, except that in some species of *Sarcophaga* the female gives birth to living larvæ and does not lay eggs.

Fig. 27.—*Sarcophaga*.



a Imago *b* Larva.

coloured larvæ or maggots (Fig. 27, *b*). The maggots

and by means of two powerful claws that are situated within the mouth, and can be protruded, are able to tear and consume all animal tissues, including soft bone, at a truly remarkable rate

As already mentioned, 1 pint of 5 per cent D D.T in orthodichlorbenzene for each 40 pounds of carcase has been suggested to control breeding. D D.T. alone is not sufficient in corpses or carcases

With a plentiful food supply and warm weather, the larvæ attain full growth in a few days, then migrate, if possible burrowing into the earth, where they pupate, emerging as flies some days later

So long as they confine their attentions merely to carcases and other decomposing material these insects may be considered harmless and excellent scavengers, but they may lay their eggs or larvæ on exposed wounds, or in the natural orifices of the body. The larvæ attack the living tissues, burrowing oftentimes deeply and causing great dam ich sometimes leads to fatal results.

Some species of *Chrysomyia*, *Sarcophaga*, etc, are obligate producers myiasis, for they are unable to live in carcases and require living tissu for development. For treatment, *see* Myiasis

HIPPOBOSCA

On horses and other animals in the East, there will often be noticed dark, flat, leathery, yellow-marked, ugly-looking flies, which at a distance resemble ticks (Fig 28)

These are the Hippobosca, which suck the blood of cattle and horses but do not attack man. They will often be found clustering under a horses' tail, and cause the animal much discomfort. When disturbed they shift about on the skin in a sidelong, crawling manner like that of a crab Occasionally they will settle on a man or his clothes, where they cling closer than a brother and give rise to a sensation of loathing They are easily caught by the hand and are best killed by pulling off their heads, their hard leathery bodies being very resistant to pressure

Fig 28 —*Hippobosca*



Melophagus ovinus, an entirely wingless hippoboscid fly, known as the sheep "tick" or "ked", transmits the non-pathogenic trypanosome of sheep, *Trypanosoma melophagium*.

NOTE.—Mention should be made of the large yellow and brown hornets

which infest Basra in Mesopotamia. They feed greedily on fæces and as, after feeding, they frequently visit water, they may pollute water supplies, possibly after these have undergone sterilization. Hence they are undoubtedly a source of danger. They are easily trapped by the methods employed for wasps in this country.

BERIBERI

Beriberi is a deficiency disease characterized by a triad of symptoms: cardiovascular disturbances, œdema, and multiple neuritis. The constant and predominant deficiency is that of vitamin B_1, also known as thiamin and aneurin. Acute forms of the disease are rapidly cured by administration of this vitamin, but various deficiencies, especially of other vitamins of the B group, probably play a part in chronic neuritic types.

Etiology.—Beriberi is endemic in areas where the chief article of diet is rice, notably in Japan, China, Malaya, the Dutch East Indies, eastern and southern parts of India, and the Philippines. It is also met with in Newfoundland and Labrador where all the flour eaten is white. The deficiency is caused by removal of the outer vitamin B-containing layers of the grain in milling Sporadic cases arise through failure to ingest or [illegible] *vitamins of the* gastro-intestinal [illegible]

Thiamin is necessary for the oxidative breakdown of carbohydrates in the body. The amount of vitamin required is in quantitative relationship to the amount of carbohydrate, so that a large demand for energy from carbohydrate food may precipitate relative deficiency when the intake of vitamin B_1 is only just sufficient for basal needs. Conversely, beriberi does not develop in starvation when the energy needs of the body are low and chiefly met by body fat, but it may appear in acute form when liberal feeding is resumed It is said that cardiac beriberi does not develop unless an individual is taking a maintenance diet of which at least 66 per cent is thiamin-free carbohydrate.

Symptoms.—The clinical picture of beriberi varies according to the relative predominance of the three characteristic features: cardiovascular disturbances, œdema, and neuritis Predominance of the first two constitutes the "wet" type of the disease, which tends to be associated with acute and severe deficiency of thiamin, whereas the neuritic or "dry" type is more frequently observed in chronic low-grade deficiency. Mixed forms are seen

Wet type.—The earliest symptom is weakness of the legs, quickly followed by tenderness of the calves. Then œdema develops in functioning muscles, making them appear enlarged. The calf muscles are affected first, later the arm muscles become involved. Some degree of subcutaneous œdema is present and the parotid glands are swollen. Short- [illegible] often accompanied by a feeling [illegible] rdiac involve- [illegible] the diastolic

Congestive cardiac failure supervenes, œdema increases, and fluid may collect in the serous cavities The heart failure is associated with a high rate of cardiac output and the extremities remain pink and warm The pulse rate is rarely above 120 a minute even in bad cases The urine, which is free from albumin in the earlier stages, may now contain albumin and casts, or urinary secretion may fail altogether Vomiting is a common terminal symptom

The electrocardiogram may show flattening or inversion of the T-wave in leads I, II, and III, shortening of the P-R interval, and prolongation of the Q-T interval

Under treatment with thiamin the diastolic pressure rises in a few hours nd a period of hyperpiesia (systolic blood pressure 140 to 160 mm Hg) sues for two or three days, then diuresis takes place and normal blood essure is restored.

nfantile Beriberi—This is a special form of the disease common in Far East It occurs in infants at the breast nine to twelve weeks old is due to diminished thiamin calorie ratio in the milk of the mother, usually does not show signs of beriberi herself The clinical picture -- vest described by Bray—disinclination for the breast with "spilling" of the milk from the mouth while water is eagerly consumed and retained, increasing restlessness, abdominal tenderness, especially over the liver, and gastric distention accompanied by colicky pain, vomiting, and paroxysmal screaming, constipation and diminution of urinary secretion, and water retention so that the infant actually gains weight There follow acceleration of the heart rate up to 200 a minute, rapid breathing, dyspnœa accompanied by a peculiar grunting, aphonia due to œdema of the larynx, cyanosis, signs of cardiac enlargement, pulmonary congestion and engorgement of the liver, fluid in the serous cavities, and generalized œdema. Later come signs of increased intracranial pressure with mening-ism, rigidity, twitchings, drowsiness, coma, and death Each phase may last only a matter of hours and the whole illness only a day or two.

Dry, Neuritic, or Paraplegic Type—This form of beriberi is characterized by ascending symmetrical peripheral neuritis Symptoms begin to appear when the intake on vitamin B_1 has been inadequate for some three months The onset is more insidious than in the wet type The first complaints are of weakness and cramps in the legs which are provoked by decreasing amounts of exercise Sensations of burning are felt in the soles, and of numbness on the dorsum of the feet and around the ankles. The ankle- and knee-jerks, after a short period of exaggeration, became diminished and eventually lost. Impairment of the power of dorsiflexion of the foot develops into foot-drop with high-steppage gait The muscles of the calves are tender on compression Hyperæsthesia, which appears as a band around the limb, is followed by anæsthesia with loss of vibration and postural sense as it ascends The muscles and skin atrophy and the limbs become emaciated

These changes in the lower limbs are followed by similar events in the upper limbs culminating in atrophy and wrist-drop There is some evidence that the priority of the paralysis may be determined by occupational stresses.

Involvement of cranial nerves, especially the second and tenth, has been recorded. Diaphragmatic paralysis may appear in severe cases.

Diagnosis.—It is of great help if a reliable and accurate history of thiamin deficiency can be obtained; unfortunately this is often impracticable in the circumstances in which cases may be met with. Administration of adequate amounts (*see* treatment) of thiamin will effect dramatic improvement in a matter of hours in acute, wet, and infantile types and it confers notable benefit in early neuritis. The thiamin content of the urine is greatly reduced in beriberi and if there are facilities for its estimation this is helpful in diagnosis.

Differential Diagnosis.—The wet type is easily confused with the weakness and œdema which occur in an anæmic individual doing hard work. Anæmia, however, is not a feature of beriberi.

Wet beriberi in its early stages is distinguished from renal disease by the absence of albuminuria, later, when cardiac failure has supervened, the very low diastolic blood pressure is a helpful point of differentiation.

Hunger œdema is distinguished by the greater laxity and dependency of the œdema and by the fact that the subcutaneous tissues rather than the muscles are affected. Moreover, beriberi is not likely to become manifest during actual starvation though it may appear after feeding is resumed.

Epidemic dropsy, which occurs in eastern India, is very similar to beriberi, it is of uncertain etiology. It may be caused by contamination of mustard oil (used for cooking) with the seeds of *Argapemone mexicana*, or it may be due to faulty or unduly prolonged storage of rice, this, without actually lowering the thiamin content, may render the vitamin more readily destructible on cooking.

Banjunans disease, which occurs in Java and is caused by eating coconut-oil cake damaged by a fungus, is characterized by transient œdema and neuritic manifestations.

The heart in the congestive failure of cardiac beriberi has a high output rate, which accounts for the warm pink extremities; in this it differs from most other forms of heart failure except that of hyperthyroidism, from which it is distinguished by absence of the other signs of thyrotoxicosis.

The dry type of beriberi must be differentiated from neuritic manifestations of other diseases. The neuropathies of alcoholic and arsenical poisoning may give rise to special difficulty because the immediate cause [illegible] Diagnosis in these [illegible] Other neurological [illegible] are tabes dorsalis, [illegible] cal pictures may be complicated by other deficiencies, especially of riboflavin and nicotinic acid, high-grade protein, and iron.

Prophylaxis.—Prevention consists in providing a balanced diet containing 1 to 2 mg. of thiamin a day. This may be attained by substituting under-milled or parboiled rice or whole-wheat flour for polished rice or white flour. If this is not practicable, other foodstuffs of high thiamin content, such as nuts, legume vegetables, and fresh meat may be intro-

duced. Another method is to supplement the diet with yeast, yeast extract, or vitamin tablets. If the dietetic habits of the people and the supply situation permit, it is better to use natural foodstuffs because these contain other important nutritional principles as well as thiamin.

Treatment.—It is essential to give adequate amounts of vitamin B_1 (thiamin, aneurin) as soon as possible. In acute cases it should be injected intravenously. The actual dosage recommended by different authorities varies from 5 to 100 mg a day, it is probably wise to give 50 mg. on the first day and continue with 20 mg a day until symptoms are well controlled, after this, thiamin may be given by mouth. Mild chronic cases may be treated with oral thiamin from the beginning

Infantile beriberi should be treated with intramuscular injections of thiamin.

In severe cases the patient may be able to take only small feeds containing marmite, but a dry, balanced, low-carbohydrate diet, enriched with all vitamins, should be instituted as soon as possible.

Cardiac failure in beriberi often responds within a few hours to intravenous thiamin, "cardiac" drugs are of little use and adrenalin is harmful, but venesection and oxygen administration may be of value in the period before the thiamin takes effect Anuria may be treated with mersalyl (salyrgan) and calcium chloride.

Absolute rest in bed is necessary for severe cases, and a considerable degree of rest is also required for mild cases; part of its value is that it reduces the demand for thiamin.

Postural rest, prevention of deformities, and later reconditioning of paralysed muscles should follow the lines adopted for other forms of peripheral neuritis.

BLACKWATER FEVER

Definition—Known also as malarial hæmoglobinuria or hæmoglobinuric fever, this condition is essentially an acute hæmolysis of uncertain causation, resulting in hæmoglobinæmia and hæmoglobinuria, and associated with inadequately treated malaria It is entirely distinct in its pathological nature and mechanism from a malarial attack, but malarial infection is an essential factor in its causation

Distribution.—It is found wherever there are hyperendemic foci of malaria, and in such places M.T. infection (*P falciparum*) is always predominant—on the West coast of Africa in the deltas of the Congo, Niger, and Gambia rivers, in East Africa along the Zambesi, in Uganda, on the upper Nile; and in Algeria In Europe, it is found in Bulgaria, Albania, Greece, and Sicily, and, of recent years, it has been increasingly common in Macedonia. In Asia, it is met with in Palestine, especially in the Jordan valley, in India, in Behar, Assam, the Dooars, and the Terai, foothill areas of the Himalayas, in Indo-China and in Formosa In America, it is found in the southern portion of the United States, in the West Indies and in Venezuela. From the Panama Canal zone it has disappeared since the introduction of anti-malarial measures.

The disease is one that attacks *visitors* to the malarial hyperendemic areas. It is rare in the indigenous inhabitants of tropical regions. These visitors need not be Europeans, *e.g.* labourers moved to build the Corinth canal, Chinese labour to build the Congo railway, Bengal clerks employed in the Punjab, have all shown a high incidence. It is possible that a marked increase in Macedonia was due to the great influx of refugees into that country after 1925. While this visiting factor is definite, there is, however, a necessary residence in the area, usually about one year. Blackwater fever not infrequently develops in England and other temperate countries in persons recently returned from areas where the disease is prevalent.

Etiology.—The conditions which conduce to an attack of blackwater fever are :—

(1) The existence of intense endemic malaria.
(2) Reinfection with malaria appears to be an important factor. It is seldom that any first infection, however severe, causes hæmoglobinuria.
(3) Residence in the endemic area has usually been over six months and under five years.
(4) The individual has usually suffered from several attacks of malaria and these have commonly been insufficiently treated. The previous attacks need not have been severe; they may have been minimal or, especially if suppressive quinine has been taken in an irregular fashion, may have been unnoticed.
(5) Heat, cold, or fatigue may precipitate an attack. Alcoholism predisposes. Other drugs have been incriminated. Pamaquin, arsphenamine, quinine, and even mepacrine have been blamed.

It must be admitted that our knowledge of the cause of this condition is defective. Of its very close association with malaria there can be no [illegible]

tick fever.

The most generally accepted theory is that blackwater is a manifestation of malarial toxicity in persons saturated *with malaria, the attack being* determined by various depressing factors or by quinine. The toxin may have hæmolytic properties, and it has been suggested that it is manufactured in the patient's body as a result of auto-immunization against his own red cells. In addition, the red cells are damaged by the malarial parasite.

There are various modifications and amplifications of this view, some laying stress on the presence of acidosis, some stating that the hæmoglobinuria is due to a hæmoglobinæmia, *i.e.* free hæmoglobin in the blood plasma, and not to a hæmolysinæmia, others considering that the administration of sulphates or of acid salts of quinine plays a part, yet others invoking a theory of anaphylaxis. Blacklock suggests that the

noxious agent is lactic acid, which he states causes hæmolysis *in vivo* and *in vitro*, and accumulates through deficient oxygenation of the blood due to anæmia.

Hamilton Fairley has shown that the pigment in the blood of cases of blackwater fever is pseudomethæmoglobin (methæmalbumin), previously wrongly described as methæmoglobin. This pigment appears in the plasma and *never* in the red cells or urine, it originates from extra-corpuscular hæmoglobin and, in fatal cases, increases progressively until death. The pigments found in the urine are oxyhæmoglobin, methæmoglobin, urobilin, and hæmatin.

Nothing certain is known except the undoubted fact that hæmoglobin is set free in such quantities that the liver cannot cope with it and convert it into bile pigment. Hence it appears in the urine. In many cases the liver is extensively damaged and in those showing anuria there is a mechanical blocking of the renal tubules by blood debris, *i.e.* hæmoglobin casts. Recent research has tended to modify earlier views on blockade of kidney tubules by debris and acid hæmatin as an important factor in the production of oliguria, anuria, and fatal uræmia—a common sequence in fatal cases of blackwater fever. More importance is now attached to other factors like "shock", peripheral circulatory failure, low blood pressure, anoxæmia and "renal anoxia", severe anæmia, dehydration, and other such features. Blackwater fever has much in common with "crush syndrome" and mismatched transfusion.

Symptoms.—The usual course of a case is as follows:—Under the conditions already mentioned the patient feels himself in the grip of what seems to be one of his old malarial chills. He realizes, however, that it is more severe than usual and he feels prostrated by it. He may have been feeling out of sorts for some days and may have noticed that his conjunctivæ have taken on a yellow tinge. On the other hand, the attack may be very sudden, the patient starting to shiver and shake, developing a headache, lumbar pain, and a nausea which soon ends in retching and vomiting of bile. He often suffers from epigastric or hypogastric pain. His temperature mounts rapidly and he finds himself passing a dark urine which may vary in colour from a reddish hue to that of black coffee and has a heavy deposit. His liver and spleen enlarge, his skin is hot and dry and soon develops a jaundiced tint which rapidly deepens. The rapid pulse soon becomes weak, compressible, and of low tension. Sometimes there is constipation, sometimes bilious diarrhœa. The symptoms increase in severity and then, in a favourable case, the skin begins to act freely, the temperature falls and the urine slowly clears, leaving the patient exceedingly weak. The hæmoglobinuria usually lasts about two days. There may be no more pyrexia, or recurrence of fever may take place next day and perhaps for several days. In bad cases the temperature runs a remittent or even a continuous course for several days. High fever, mental confusion, persistent vomiting, hiccup, profuse diarrhœa, and a diminution in the quantity of urine passed are bad signs. Blackwater fever cases usually die from hæmolysis, anuria, or hyperpyrexia with coma. The hyperpyrexia may set in after the urine has entirely cleared.

The great derangement in liver function which occurs should be borne in mind, as the jaundice and some of the cerebral symptoms are probably due to this cause.

Four clinical types of the disease are described.

(1) *Mild to moderate uncomplicated type.*—This accounts for the majority of cases seen. Hæmoglobinuria is definite, the colour of the urine varying from bright red to dark brown, and may last from a few hours to about three days. The intensity of the hæmoglobinuria is usually greatest at first and gradually diminishes. The amount of urine passed is usually normal. If, in treatment, a large amount of fluid is

[illegible]

falls to normal. Vomiting may or may not occur, and icterus and subsequent anæmia are slight. There is no anuria and toxic manifestations are few. Recovery is the rule.

[illegible]

polyuric condition develops, each specimen of urine showing more

[illegible]

tends to drop. Hiccup is marked and delirium common before death, which may occur very soon. In a case which survives more than twenty-four hours, jaundice is intense and the anæmia is profound.

(3) *Anuric type.*—The anuria which may develop in a first or subsequent attack cannot be anticipated. It may appear early or late—usually early. When suppression occurs there is almost total anuria, but usually 50 to 100 c.cm. of urine may be obtained by catheter. The urine thus obtained is bile-stained and, from the high degree of albuminuria, has the appearance of serum rather than of urine. The temperature falls after the initial pyrexia and tends to remain subnormal. Since the whole burden of disposing of the hæmoglobinæmia has fallen upon the liver, the gravest degree of icterus is seen in this type. Life, in these cases, is often surprisingly prolonged up to the eighth or tenth day. In spite of high nitrogenous retention, uræmic symptoms may not appear, and the patient, far from being comatose, may be mentally alert. Vomiting is usually severe, but it may cease a few days before death. Occasionally the liver would seem to have been able to compete with the hæmoglobinæmia and the icterus may clear up.

(4) *Continued or intermittent type.*—In this type the hæmoglobinuria clears up only to recur or it may be continuous. With continued or [illegible] Oliguria is not seen [illegible] miting and hiccup [illegible] The anæmia is [illegible] mostly to recover.

There is apt to be a run of comparatively mild cases ending favourably and then a series of severe cases, every one of which may prove fatal. Hence caution must be exercised in attributing success to any special line of treatment

Morbid Anatomy.—As explaining the symptoms it is well to mention that the chief pathological findings are those of malaria, but that focal necroses of the liver and spleen suggest the presence of a toxin. The bile is inspissated, the kidneys enlarged and congested with deep purple pyramids. The tubular epithelium is degenerated and the tubules choked with granular material and hæmoglobin casts.

The urine shows a copious granular sediment, the nature of which has not been definitely determined. Hæmatoidin crystals may be present and occasionally, but rarely, a few red cells.

Complications.—The passage of blood or hæmoglobin from the bowel may be mentioned.

Diagnosis.—The condition of the urine is the chief guide. It has usually been taught that while malarial parasites may be found in the peripheral blood before the attack, they disappear once the hæmoglobinuric condition is fully established, or at least are very difficult to find. There can be little doubt that such a view requires some modification, for if the thick film method is employed, the percentage of success in the discovery of the parasites will materially increase. At the same time, there are cases where the blood is apparently free from plasmodia; and, indeed, an attack of blackwater may actually cure a malarial infection by breaking down the host cells and wholly destroying the intracorpuscular parasites.

When parasites are present, they are usually scanty. Cases of *P falciparum* infection with high fever and large numbers of parasites in the peripheral blood do not, as a rule, develop blackwater fever. Cases are recorded in which only *P. vivax* and, in a few cases, only *P malariæ* parasites have been found, and these species have been incriminated as causative, but it is generally believed that the disease is due only to *P. falciparum* infection, even although the parasites may be so scanty as not to be found after repeated examination of thick and thin smears.

Differential Diagnosis.—This is not difficult save in paroxysmal hæmoglobinuria, which appears to be uncommon in tropical countries, in a hæmoglobinuric condition induced by quinine alone or pamaquin alone—both rare events—and in sickle-celled anæmia Bilious remittent fever is a severe form of malaria in which there is jaundice and liver failure and in which the urine is dark owing to bile, but here, as in the case of yellow fever, leptospiral jaundice, and infective hepatitis, the cardinal sign of blackwater, namely hæmoglobinuria, is absent

Favism may have to be distinguished from blackwater fever It is an allergic form of hæmoglobinuria due to ingestion of the broad bean (horse bean), *Vicia faba*, or to inhalation of its pollen during the flowering season in April–May. Favism is a sporadic disease and it is found in certain areas bordering the Mediterranean Because most of these areas are also malarial, and the clinical picture of favism is very like that of blackwater

... may arise unless the possibility is borne in mind.
... of hæmoglobinuria has occasionally ... Force) in patients under treat- ... attack, usually a mild one, of ment with pama... ... plication has usually appeared benign or subtertian malaria. This ... course of pamaquin (0 01 g. thrice towards the end of the normal five-day course of pamaquin (0 01 g. thrice daily) or shortly after its completion. In most cases the patient has already completed the quinine and mepacrine stage of the standard course without incident. It is uncertain whether this is true blackwater fever, pamaquin havin... a trigger, or whether the drug itself has been wholly res... ... hypothesis that the great majority of ... ...us complication have long been resident in highly ... and that recent arrivals from non-malarious countries (i e. British troops from the United Kingdom) have not so far suffered from these attacks although many thousands of them have had the standard course of quinine, mepacrine, and pamaquin.

Prognosis.—The fulminating toxic types end fatally. Anuria is always serious Cases with intermittent attacks of hæmoglobinuria and rigors are also apt to do badly, in these jaundice is slight but anuria frequent. In ordinary cases a great deal depends on the patient's surroundings and how he is nursed. The medical officer should never abandon hope. If he does not spare himself and proceeds on the lines indicated he may have the satisfaction of seeing even a very grave case recover.

Prophylaxis.—Malaria prophylaxis is also the method to prevent black- water. The introduction of an effective mepacrine dosage for malaria suppression (0 1 g daily) has completely revolutionized the blackwater fever situation. As a direct result of the introduction of this regime, blackwater fever has become a rare disease in many parts of the world where it was once common. Even on the West Coast of Africa, where it was once among the chief dangers to the health and lives of European visitors, blackwater fever has almost disappeared. A small number o cases must still be expected so long as there are some who, for variou reasons, fail to take mepacrine regularly in sufficient dosage—an essent precaution in any country where blackwater fever is to be expecte Mepacrine must be continued for four weeks after leaving the malari area.

For the present it is the policy that soldiers who have once suff from blackwater fever will not again visit an endemic centre of the di if this can be avoided In the light of the recent demonstration o great value of mepacrine in preventing blackwater fever, it may be possible to relax the rules forbidding return to the tropics after an a

Treatment.—In every case, no matter how slight, this spells a rest in bed and skilled and careful nursing. If it can possibly be a blackwater patient should never be moved from the place wh taken ill. So long as he has a bed to lie on, a roof to cover him, a sensible person to look after him who will carry out the doctor he should be treated on the spot. Under war conditions this is, not always possible, but the medical officer should always weig

and cons most carefully before ordering a patient to be transferred to a hospital at any distance. It is better, when it can be arranged, for the nurse to go to the patient than for the patient to come to the nurse.

It has recently been shown that the oliguria, which is so often a dangerous complication of blackwater fever, is not the result, but rather the cause, of blockage of the renal tubules by insoluble crystals of acid hæmatin, and that drastic measures to render the urine alkaline, besides failing in their purpose, may produce a dangerous state of alkalosis even while the urine remains strongly acid. On this account it is inadvisable to push alkalies in the treatment of this disease.

To combat the blood loss and to provide adequately functioning red cells to maintain the urinary secretion, blood transfusion has been found of the greatest value, especially in the polyuric type and in those showing repeated or continued hæmolysis, but it must not be undertaken in the presence of anuria. The blood used must be absolutely compatible and cross-matching is essential, since incompatibility itself produces hæmolysis and in severe hæmolytic states the red cells are prone to auto-agglutination. From 300 to 500 c.cm. of citrated blood are given, best as a straight transfusion, and repeated as required. Where there is a risk of embarrassing the circulation by the sudden introduction of a relatively large volume of fluid, the transfusion may be given by continuous drip extending over several days. Packed red cells may also be used with the same end in view. Transfusion has no effect on the hæmolytic process and the transfused cells are hæmolysed as readily as the patient's own. Its value lies in providing functioning red cells as required. Anti-coagulants are of little if any value.

Diuretics which stimulate the kidneys must be avoided. Sufficient flushing of the kidneys may be secured by administration of fluids by the mouth In addition to the alkaline drinks already mentioned, the patient should be encouraged to take as much water, tea, barley-water, or raisin tea (*see* p. 97) as possible. If this endeavour fails to accomplish its purpose, recourse may be had to saline injections. As an alternative to the intravenous infusion already described, saline may be given per rectum, *six or eight ounces of physiological salt solution being administered if necessary every hour or even oftener, or preferably by rectal drip.*

[illegible]

hallucinations. His muscles twitch and tremble, and delirium, usually of a low muttering type, ensues. There may be convulsions and coma. In such cases the effect of glucose should be tried. Apart from the raisin [illegible]

be used in 10 per cent. solution.

As mentioned above, as soon as the stomach can tolerate food a fluid diet should be given in the form of whey, albumin water, milk, chicken

broth and Benger's food. Raisin tea, on account of the sugar it contains and the fact that it is often well retained, is useful. In certain cases recourse may be had to rectal feeding. It is very necessary to guard the patient against chill for nephritis is apt to follow blackwater and patients who recover from hæmolysis sometimes die later from chronic Bright's disease.

Frequent sponging may be useful. If suppression threatens, wet or dry cupping and the application of poultices or hot fomentations to the loins can be tried.

The tendency to cardiac failure is best combated by strophanthus, digitalin, or pituitary extract and the patient should not be allowed to sit up in bed. When vomiting is bad the stomach may with advantage be washed out with bicarbonate of soda solution. Ice, tincture of iodine (3–5 drops in a little water), sips of very hot water, or a dose of morphine, may check it, but probably the most effective treatment is champagne, iced if possible, taken in small sips. Constipation must be prevented.

For restlessness and pain in the back and legs morphine, hypodermically, is often invaluable, but it must be given cautiously and in small doses. Cold applications to the head and especially behind the ears alleviate headache. After an attack the patient is very weak and anæmic. He requires careful feeding and tonics, especially iron, as soon as the acute symptoms have ended, iron and ammonium citrate gr. 40 t.d s. may suitably be prescribed. It is advisable that he should be invalided out of the endemic area, and he should be specially warned as to the danger of getting chilled or wet.

As quinine is often the "trigger that fires the gun" of blackwater fever it is better withheld. Mepacrine may be given cautiously to those showing parasites in the peripheral blood, and even when no parasites have been found, mepacrine treatment should be commenced a few days after hæmolysis has ceased.

For the same reason pamaquin has no place in the treatment of blackwater fever even if malaria parasites are found in the blood. An attack of malaria is apt to develop a few days after the blackwater has subsided. This attack is best treated with mepacrine, beginning with small doses as recommended and gradually working up to the full dosage. Quinine anc pamaquin should be omitted for the reasons already stated.

Treatment may be summarized as follows:—

(1) Absolute rest in bed, even for the mildest cases; skilled and caref nursing.
(2) Do not move the patient if it can be avoided.
(3) Protect the kidneys by giving fluids and alkalies, but not to exce
(4) Combat the anæmia by transfusion.
(5) Treat the malarial infection with mepacrine.

CEREBRO-SPINAL FEVER

Introduction.—Cerebro-spinal fever is an infectious disease of central nervous system. It arises when the causative organism meningococcus, having invaded the blood stream attacks the men brain, or spinal cord.

The disease is variously known as cerebro-spinal fever, cerebro-spinal meningitis, meningococcal meningitis, posterior basal meningitis, spotted fever.

In England the academic name for the meningococcus is the *Neisseria meningitidis*, whereas in America the term *Neisseria intracellularis* is employed. In view of the fact that the organism is by no means always seen within the leucocytes the English name is considered to be more truly descriptive.

The commonest site of infection with the meningococcus is the nasopharynx, where it may give rise to a rhinopharyngitis, but in most cases no visible lesion is evident. The organism may therefore be readily transferred from person to person through aerial projection of infected droplets and the infection may become widespread throughout a community without, of necessity, giving rise to obvious disease.

Under certain conditions the organism may invade the blood stream of individuals and attack the central nervous system to give rise to cerebro-spinal fever. On occasions the nervous system escapes and the disease is restricted to a meningococcal septicæmia.

The factors that influence the invasion of the blood stream are still imperfectly understood, and although the invasion may be associated with changes in certain characteristics of the infecting strain of organism it is undoubtedly largely a matter of individual susceptibility. There is much evidence to suggest that this susceptibility is produced, or at any rate increased, by fatigue and recent infections of the upper respiratory passages.

Experience has shown that it is rare for a contact of a case to develop the disease. During periods when the incidence of the disease is generally increased, as many as 70 per cent. of the population may be found to be harbouring the meningococcus without showing evidence of disease and the very extensive investigations undertaken during the 1914–18 war pointed to the fact that almost every case of cerebro-spinal fever was contracted from healthy individuals harbouring the organism. Further work carried out since then has confirmed these observations.

Cerebro-spinal fever may occur in individuals of all ages, and of either sex, but young men lately transferred from civil to military life appear to be especially prone to attack.

Clinical Considerations

Incubation Period.—The incubation period is indefinite. It may sometimes be as short as twenty-four hours and may be extended to as long as ten days or even longer, but the common period appears to be between three and five days.

Signs and Symptoms.

(i) *Stage of Invasion.*—This may be very brief, lasting a few hours only, but may go on for a week or more. The onset is apt to be sudden with malaise, moderate headache, fever, perhaps vomiting, and occasionally a petechial rash.

(ii) *Involvement of the Nervous System.*—As the brain and meninges become affected the headache becomes intense and intolerable. The

drowsiness deepens and the patient can only be aroused with difficulty. Vomiting increases and there is pain and stiffness of the neck. Meningeal reactions may be presumed as soon as the neck stiffness is evident or Kernig's sign unequivocal.

Clinical Types.—*The clinical picture of cerebro-spinal fever is* very varied and may range from the mild abortive case to the very severe and rapidly fatal type. Although no clear-cut division can be made between the various types they are discussed for the sake of simplicity under three headings —

(i) *Mild or abortive type* in which malaise, possibly some "pharyngitis", moderate headache, and slight fever may be associated with some stiffness of the neck.

Spontaneous recovery may occur within seven to eight days and meningeal involvement may not be appreciated clinically. The true nature of the disease may only be demonstrated after the laboratory investigation of the cerebro-spinal fluid.

(ii) *Average Type.*—The temperature and pulse rate are very variable. A rash may or may not be seen; when noticeable it is generally petechial. Vomiting is the rule. Effusions into the joints, myalgia, twitchings, or muscular spasms may all be seen. The headache, at first frontal, later becomes general and agonizing. The patient may be drowsy, stuporous, restless, and delirious or may be extremely irritable and resent all interference The eye- and face-muscles may be affected and deafness also is not uncommonly noted.

As the meningitis develops the patient settles into the characteristic decubitus, lying on the side with the back to the light, knees drawn up, and neck extended. Unconsciousness and incontinence develop

(iii) *The Very Severe or Fulminant Type.*—The attack may be so overwhelming that the patient may die within twenty-four or forty-eight hours without headache or any signs of meningitis. There may be an extensive purpuric eruption, bleeding from mucous membranes and perhaps pain and collapse from a terminal hæmorrhage into the suprarenal medulla.

On the other hand the patient may die of an acute encephalitis with violent headache, vomiting, early coma, and only slight fever.

(iv) *Sub-acute Meningococcal Septicæmia with or without Meningitis.*—In some patients the signs and symptoms may be limited to a moderate fever with skin lesions, and muscle- and joint-pains. Meningitis may develop only after many days, weeks, or even months, or not at all. The skin lesions may be petechiæ, rose-red [illegible] patches or painful and tender pinkish nodes. [illegible] blood during each recurrence.

Diagnosis.—Although a clinical diagnosis of cerebro-spinal fever may

be presumed in the presence of the classical signs and symptoms, especially during an outbreak of the disease, the only accurate method of diagnosis is the demonstration of the meningococcus in the cerebro-spinal fluid or blood

The cerebro-spinal fluid is usually under increased pressure and on occasions markedly so, but the increase is not always obvious without a manometer reading In the early stages of the infection the fluid may be clear, but in most established cases it is turbid or frankly purulent. Even where the fluid is clear to the naked eye there will be an increase in the cell count with the majority of the leucocytes of the polymorphonuclear variety and the sugar content less than normal

A careful examination of suitably-stained smears will usually demonstrate the presence of gram-negative intracellular diplococci, but on occasions they may be very difficult or impossible to find. In some very severe cases or in patients whose condition is rapidly deteriorating the cerebro-spinal fluid may show only extra-cellularly placed meningococci.

The infecting organism may be cultivated from the cerebro-spinal fluid of untreated cases on almost every occasion, even when it cannot be demonstrated in direct preparations, and the true identity established by serological analysis of the culture

At the same time blood cultures taken early in the disease, in a large proportion of the cases, result in the recovery of the meningococcus. Patients suffering from chronic meningococcal septicæmia may also yield positive blood cultures during the early stage of the infection or at the beginning of a relapse, but repeated blood culture is often necessary before success is obtained.

But a large proportion of the patients will have received sulphonamide therapy before culture of cerebro-spinal fluid or blood can be carried out, therefore the successful recovery of the meningococcus cannot be so readily assured as it was before the introduction of this group of drugs. In order to overcome the bacteriostatic effect of the sulphonamide derivatives the addition of para-amino-benzoic acid (5 mg per 100 c.cm) to the cerebro-spinal fluid or the blood-culture medium is recommended.

During the early stages of cerebro-spinal fever meningococci can usually be recovered from the posterior nares and in the great proportion of the cases will be found to belong to the same serological group as those infecting the meninges While such findings may not be of absolute diagnostic value they are sufficiently constant to be of some significance.

Differential Diagnosis.—Although during the period of increased general incidence the early recognition of cerebro-spinal fever may be simple, it is well to remember that it is clinically impossible to differentiate with certainty between cerebro-spinal fever and any other form of pyogenic meningitis. Of other forms of meningitis, the tuberculous form usually has a slower onset, but acute benign choriomeningitis, meningitic forms of acute anterior poliomyelitis and encephalitis lethargica or post-vaccinal encephalitis may be mistaken for cerebro-spinal fever.

In the fulminant cases the patient may be quite unconscious when first seen. During an outbreak, the possibility of cerebro-spinal fever must

always be considered [illegible]

[illegible] ditions, influenza, typhoid, undulant fever, miliary tuberculosis, erythema nodosum, subacute bacterial endocarditis, rheumatic fever, gonococcal septicæmia, relapsing fever, sleeping sickness and heat-stroke may have to be considered.

Lumbar Puncture

The diagnosis of cerebro-spinal fever depends upon the demonstration of the meningococcus in the cerebro-spinal fluid withdrawn by lumbar puncture. This procedure may, at the same time, have an immediate therapeutic value in relieving the intolerable headache, and possibly the vomiting also, induced by the increased tension of the fluid. The pressure of the fluid in a normal individual varies between 100–180 mm. of water, but in a developed case of cerebro-spinal fever may rise to as high as 300 mm. It is important, therefore, that decompression should be slow and to obviate the risks associated with a too-rapid lowering of the pressure it is desirable to have a manometer attachment fitted to the lumbar puncture needle.

Anæsthesia.—Patients suffering from cerebro-spinal fever may be so stuporous that lumbar puncture may be undertaken without any form of anæsthesia; nevertheless numbers are fully conscious or so irritable that they resent such procedures. If the operation is to be carried out with ease and success it is essential to obtain adequate flexion of the spine and to ensure against sudden movements of the patient. In the majority of cases, therefore, some form of anæsthesia is an advantage.

It is usually sufficient to employ local anæsthesia in the form of an injection of 2 per cent. procaine and adrenaline in the operation area. General anæsthesia is employed much less frequently to-day than previously, but there are occasions, such as certain cases of delirium or where there is spasm of the extensor muscles, where it may be useful. An intravenous injection of pentothal sodium is suitable for this purpose. A general anæsthetic should be avoided, however, whenever possible.

Apparatus Required for Lumbar Puncture.—Standard lumbar puncture needles, with manometer and connecting rubber tubing, if available.

Sterile test-tubes plugged with cotton wool.

Iodine.

Swabs.

Adhesive strapping.

Sterile towels.

Technique of Lumbar Puncture

Preliminaries.—Successful lumbar puncture is largely dependent on the patient being in the correct position. The patient should lie on his side on a reasonably flat bed with the trunk flexed so that the lumbar spine is convex backwards and not rotated. The buttocks should be moved to the edge of the bed, and the trunk, neck, and knees well bent, with the shoulders and pelvis vertical. If the operation area is hairy it should be shaved, washed, and dried. Having placed the patient in the correct

position an assistant should ensure its maintenance by placing one arm round the shoulders and the other under the bent knees. The lower lumbar and upper sacral region is swabbed with iodine and one sterile towel is placed over the buttocks and another on the bed under the lower buttock.

If an anæsthetic is to be used this procedure is now carried out.

The operator's hands should be surgically clean and dry The lumbar puncture needle and accessories should be removed from the sterilizer, drained of water, and allowed to dry as much as possible.

Operation.—The site for the insertion of the needle is now defined. The best point for this is in the middle line between the 3rd and 4th or 4th and 5th lumbar spinous processes. The 3rd to 4th space lies on a horizontal line joining the crests of the ilia. Having chosen the space that provides the larger gap the operator places the tip of his left index finger on the upper part of the lower spinous process and inserts the needle, with the stylet in position, into the lower part of the interspinous space in the middle line. The bevelled edge should be in the longitudinal axis of the spine in order to diminish the chance of cutting the fibres of the ligaments.

The needle should be pushed through the skin quickly and then slowly directed forwards and slightly upwards, feeling the way for any obstruction If bony resistance is encountered it is withdrawn a little and directed somewhat higher With experience the sense of touch will often tell when the needle has reached and pierced the ligamentum subflavum, some 5 cm from the surface in an average adult. When the operator judges that this barrier has been passed it is advisable to remove the stylet and see whether C S F. runs out. It is well not to go too far, for the needle may easily enter the venous plexus in front of the spinal canal and thus contaminate the fluid with blood. A "dry tap", on the other hand, usually means that the [illegible]

manometer and its pressure is read on the millimetre scale. (The patient if fully conscious should be told to breathe easily, for irregularities in respiration may raise the pressure) If the pressure is about 100 mm, fluid is allowed to escape until it reaches that level—but never faster than a quick drip. Two samples of about 5 c cm each are then collected in

TREATMENT

Sulphonamides are now the basis of treatment for meningococcal infections, though penicillin is equally effective if correctly used, other measures, such as the use of antiserum have now been superseded The mortality and morbidity of the disease has greatly diminished. With

early administration of sulphonamides in adequate dosage, bacteriostasis should be complete within 12 to 24 hours. Early recognition of cases is always of first importance. Lumbar puncture is necessary for diagnosis but the procedure need not be repeated unless it is needed for drainage or the relief of pressure. Symptomatic treatment and the need for expert nursing must not be overlooked: hot baths for pain and restlessness; ice

intense pain.

Sulphonamide Treatment.—In all severe cases, including those that come under treatment late in the acute stage, the first dose or doses should be

never be practised. In order of choice, the compounds recommended are sulphathiazole or sulphadiazine, sulphapyridine, and sulphanilamide, the last being effective but less potent than the other three. The average *course of treatment lasts nine days; the general plan is to follow the*

fluids must also be given by parenteral injection, nasal tube, or rectum if they cannot be taken by mouth.

If vomiting occurs within half-an-hour of an oral dose, the dose should be repeated (*see* also p. 319). Failure to respond to the above dosage schedule usually means that the concentration in the spinal fluid has not reached the required amount of 3 to 5 mg per 100 c.cm. This point should be checked by estimation of the level and the dosage should be revised if necessary. When taking samples of spinal fluid for estimation of sulphonamide, novocain (or other local anæsthetics of the procain

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sev.

by small doses (2 grams) of sulphadiazine or sulphathiazole administered *to all in the affected community for a period of two or three days.*

PROGNOSIS

Cerebro-spinal fever must always be regarded as a grave disease for, in the absence of early and adequate treatment, the mortality is extremely high. Nevertheless, apart from the fulminant types and certain rare

complications, early treatment with sulphonamides in the correct dosage has greatly reduced the mortality.

PREVENTION

Experience has shown that it is rare for cerebro-spinal fever to be spread by patients actually suffering from the disease. When two or three cases occur in a group of individuals in contact with each other the evidence suggests that the disease is contracted from those harbouring the meningococcus but not suffering from cerebro-spinal fever.

Nevertheless the patient is, theoretically, a source of infection and should therefore be isolated if possible. The first practical step in prevention is the early diagnosis and treatment of the disease as it occurs. The medical officer who makes a clinical diagnosis of cerebro-spinal fever should take action in the following order of priority:—

(1) Make arrangements for the immediate treatment of the patient as outlined on p. 73, and also for the admission of the patient to hospital. If no isolation hospital is close at hand the patient should be admitted to the nearest military or civilian hospital with good facilities for treatment, nursing and laboratory investigations.

(2) Ensure that full records of the case together with a note of the remedies given, dosage, and times of administration accompany the patient to hospital.

(3) Make arrangements for the disinfection of clothing, bedding, and any articles that may have been soiled by discharges from the patient's nose or mouth. The meningococcus is a delicate organism and does not remain viable outside the body for any length of time and it is sufficient to wash the floor and furniture in the vicinity of the bed with soapy water.

(4) The medical officer who diagnoses the case is responsible for its notification on A.F. A 35 (notification of infectious diseases), which should be completed in all detail. The original will be retained as an office record. A copy will be forwarded through the usual channels to D.D.M.S. command or corps, or the A.D.M.S. of area, district, or division, whichever formation is immediately responsible for the unit with which the patient served. A copy will also be sent to the officer in medical charge of the effective troops or military families concerned. Should the diagnosis be made by either of these officers a copy will be sent to the military hospital receiving the patient, if the case was admitted to this type of hospital. In addition the local civil health authorities will be informed.

Officers in medical charge of effective troops among whom the patient served are responsible for the health of the remaining troops, and they should take the earliest steps to investigate conditions associated with any outbreak.

Carriers can be eliminated by small doses of sulphadiazine or sulphathiazole given over a limited period to the whole community involved. This has greatly simplified the problem of dealing with carriers, and their bacteriological examination and segregation is no longer necessary; it probably never did much good. In American trials, two grams of

sulphadiazaine for two or three days were effective in reducing the carrier state to very small proportions and in preventing fresh cases. Sulphathiazole should be equally effective.

General Preventive Measures.—Meningococcal infections may be conveyed from person to person by naso-pharyngeal discharges ejected from the nose and mouth of patients suffering from cerebro-spinal fever or meningococcal rhino-pharyngitis or healthy carriers. Cross-infection may be direct at close range from mouth to mouth or may be air-borne over distances of 20 to 30 feet in the case of the finer droplets. Close-range infection may occur in the open air or within buildings, but it is probable that the finer droplets cause infections only within buildings. Satisfactory washing-up arrangements in messes and canteens are necessary to avoid the spread of infection. These should include plenty of hot water and disinfection of crockery and cutlery by means of water-sterilizing powder.

From available evidence it would appear that the healthy carrier or the individual with a meningococcal rhino-pharyngitis is the main source from which the infection is spread.

Although the carrier rate may be high during an outbreak this is not invariably so.

During periods in which the general incidence of the disease is raised it is important to observe any measure that may contribute towards lessening the chance of infection and increase the chance of recovery of those who contract the disease.

The use of sandfly nets as filters for droplets has been suggested.

Early Recognition.—Medical officers should give short talks to regimental officers and senior N.C.Os. on the disease and the method of spread. *They should, above all, encourage all ranks to report "sick" immediately if they are suffering from headache, soreness of the throat, etc.* Furthermore, their interest should be enlisted in the further hygienic measures outlined below.

Overcrowding.—Although cerebro-spinal fever may be justly regarded as a disease associated with institutional life the original view that the increased incidence was due to overcrowded dormitories has not been *fully substantiated in the light of present knowledge.* That overcrowding is a most important factor in the spread of the disease is, in all probability, correct But however generous may be the spacing out of beds, as long as individuals are crowded together at narrow tables in lecture rooms, [illegible]

that each man sleeps next to his neighbour's feet.

Under peace conditions each person should be allowed 60 square feet of floor space and there should be 6 feet between beds.

The most dangerous periods in dormitories are during the going-to-bed and getting-up times. Unless a number of the occupants are suffering from coughs the projection of infected droplets is much less during sleep.

It is important to prevent overcrowding in dining-halls; under epidemic conditions men should if possible sit on one side of dining-tables only.

Ventilation.—All occupied rooms, including barrack-rooms, institutes, dining-rooms, lecture-rooms, etc., should at all times be so ventilated that there is a free circulation of air. As the maximum intensity of the occupation of buildings by the soldier occurs during winter evenings particular attention must be paid to the provision of a sufficiency of efficient ventilator openings. Rooms should be adequately aired to prevent dead-space air from accumulating, and suitable forms of louvred shutters must be provided to ensure ventilation in any circumstances where lights may have to be blacked-out.

The provision of adequate ventilation may not be an easy matter in some buildings, but it is the duty of all C.Os. to make every effort to see that the best ventilation possible is obtained in every occupied room. In order to ensure that satisfactory ventilation is maintained constant inspection by officers or senior N.C.Os. is necessary.

Efficient heating of occupied buildings and an adequate supply of blankets for the beds during the cold weather is essential, otherwise all efforts to maintain satisfactory ventilation will be circumvented.

Every effort should be made to deal with dust, floors should be oiled with spindle-oil

Outdoor Life.—Meningococcal infections are most readily transmitted when people are crowded together in ill-ventilated rooms During epidemic periods as much time as possible should be spent in the open air away from canteens, cinemas, and other likely sources of infection

the nasopharynx.

Sequelae, and their Treatment

Focal nervous symptoms developing during the course of the disease are not common and most of them are transient. They include cranial-nerve palsies, for example, of the 3rd, 6th, 7th or 8th, visual impairment, epileptiform seizures, aphasia, monoplegia or hemiplegia of cerebral origin, paraplegia from myelitis, and atrophic palsies with or without sensory loss due to spinal-root lesions. Some degree of weakness from hemiplegia, paraplegia, or spinal-root involvement may persist, but improvement tends to continue for months. Deafness, of varying severity, unilateral or bilateral, from neuritis of the auditory nerve is frequently, but not invariably, permanent It occurs in about 5 per cent. of cases.

In the complete syndrome the complaints are of *headache*, *giddiness*, minor mental and emotional disturbances, alteration in personality, insomnia and fatiguability, a clinical picture which closely

sulphadiazaine for two or three days were effective in reducing the carrier state to very small proportions and in preventing fresh cases. Sulphathiazole should be equally effective.

General Preventive Measures.—Meningococcal infections may be conveyed from person to person by naso-pharyngeal discharges ejected from the nose and mouth of patients suffering from cerebro-spinal fever or meningococcal rhino-pharyngitis or healthy carriers. Cross-infection may be direct at close range from mouth to mouth or may be air-borne over distances of 20 to 30 feet in the case of the finer droplets. Close-range infection may occur in the open air or within buildings, but it is probable that the finer droplets cause infections only within buildings Satisfactory washing-up arrangements in messes and canteens are necessary to avoid the spread of infection. These should include plenty of hot water and disinfection of crockery and cutlery by means of water-sterilizing powder.

From available evidence it would appear that the healthy carrier or the individual with a meningococcal rhino-pharyngitis is the main source from which the infection is spread.

Although the carrier rate may be high during an outbreak this is not invariably so.

During periods in which the general incidence of the disease is raised it is important to observe any measure that may contribute towards lessening the chance of infection and increase the chance of recovery of those who contract the disease.

The use of sandfly nets as filters for droplets has been suggested.

Early Recognition.—Medical officers should give short talks to regimental officers and senior N.C.Os. on the disease and the method of spread. *They should, above all, encourage all ranks to report "sick"* immediately if they are suffering from headache, soreness of the throat, etc. Furthermore, their interest should be enlisted in the further hygienic measures outlined below.

Overcrowding.—Although cerebro-spinal fever may be justly regarded as a disease associated with institutional life the original view that the increased incidence was due to overcrowded dormitories has not been *fully substantiated in the light of present knowledge.* That overcrowding is a most important factor in the spread of the disease is, in all probability, correct But however generous may be the spacing out of beds, as long as individuals are crowded together at narrow tables in lecture rooms, [illegible]

between the centres of beds was 5 feet. Should it be necessary to reduce the space to this minimum every alternate bed should be turned round so that each man sleeps next to his neighbour's feet.

Under peace conditions each person should be allowed 60 square *feet of floor space and there should be 6 feet between beds.*

The most dangerous periods in dormitories are during the going-to-bed and getting-up times. Unless a number of the occupants are suffering from coughs the projection of infected droplets is much less during sleep.

It is important to prevent overcrowding in dining-halls, under epidemic conditions men should if possible sit on one side of dining-tables only.

Ventilation.—All occupied rooms, including barrack-rooms, institutes, dining-rooms, lecture-rooms, etc, should at all times be so ventilated that there is a free circulation of air. As the maximum intensity of the occupation of buildings by the soldier occurs during winter evenings particular attention must be paid to the provision of a sufficiency of efficient ventilator openings Rooms should be adequately aired to prevent dead-space air from accumulating, and suitable forms of louvred shutters must be provided to ensure ventilation in any circumstances where lights may have to be blacked-out.

The provision of adequate ventilation may not be an easy matter in some buildings, but it is the duty of all C Os to make every effort to see that the best ventilation possible is obtained in every occupied room. In order to ensure that satisfactory ventilation is maintained constant inspection by officers or senior N C Os is necessary.

Efficient heating of occupied buildings and an adequate supply of blankets for the beds during the cold weather is essential, otherwise all efforts to maintain satisfactory ventilation will be circumvented.

Every effort should be made to deal with dust, floors should be oiled with spindle-oil

Outdoor Life.—Meningococcal infections are most readily transmitted when people are crowded together in ill-ventilated rooms. During epidemic periods as much time as possible should be spent in the open air away from canteens, cinemas, and other likely sources of infection If weather permits, men should sleep and eat out of doors. At the same time, it must be remembered that over-fatigue and long periods without hot meals should be avoided, as young recruits may thus become liable to colds and other minor disabilities that may render them susceptible to a blood-steam invasion of the meningococcus, should this organism reach the nasopharynx.

SEQUELAE, AND THEIR TREATMENT

Focal nervous symptoms developing during the course of the disease are not common and most of them are transient. They include cranial-nerve palsies, for example, of the 3rd, 6th, 7th or 8th, visual impairment, epileptiform seizures, aphasia, monoplegia or hemiplegia of cerebral *origin*, paraplegia from myelitis, and atrophic palsies with or without sensory loss due to spinal-root lesions. Some degree of weakness from hemiplegia, paraplegia, or spinal-root involvement may persist, but improvement tends to continue for months. Deafness, of varying severity, unilateral or bilateral, from neuritis of the auditory nerve is frequently, but not invariably, permanent It occurs in about 5 per cent of cases.

General nervous symptoms are more frequent, a fact which has only recently become recognized The highest proportion of cases occur *in*

resembles that which often follows head injury. The basis of it, from whichever cause, is organic cerebral damage, but it is often complicated and perpetuated by psychogenic factors resulting from anxiety, an appreciation of change in physical and mental state, or a desire to use invalidism for selfish ends. Such psychological complications are more liable to develop in those with a previous history of unstable temperament and neurotic illness.

Up to the present experience has shown that recovery is, in the majority of cases, to be expected, but it is believed that results would improve if the conditions were early recognized and convalescence suitably planned. At the important stage when the patient is still in hospital points of practical value have to be kept in mind by the medical officer.

(i) Headache, giddiness, fatiguability and other symptoms of the syndrome, as in the case of head injury, may be absent so long as the patient is in bed or even under the restricted conditions of ordinary hospital life. They may appear only when more normal activities are attempted. For this reason, before patients are discharged from hospital and their immediate disposal decided, their mental, emotional, and physical stamina should be tested unobtrusively. Thus, their response to reading, noise, the cinema, games, and other forms of exercise should be investigated.

(ii) Since the symptoms are subjective and usually unsupported by

and efficiency as a soldier. Care must be taken during the inquiry not to suggest symptoms

(iii) If symptoms which constitute real disabilities are neglected and the patient is prematurely sent back to duty, worry and resentment may well develop and delay or prevent recovery.

Patients who, at the end of two or at most three weeks' convalescence in hospital, still complain of disabling symptoms should be sent to ... a reablement can be provided. An aimless ... laziness and

... resemble the ... m which tests ... the symptoms ... damage, and ... be recognized by those familiar with them, the

possibility of such sequelæ nor to be obsessed by them. He must, in fact, evaluate the whole situation in each case on the available evidence and it will often be necessary to take some trouble to get it.

Further investigation into the frequency, treatment, and prognosis of

nervous sequelæ of cerebro-spinal fever in soldiers is necessary, and for this purpose all patients before they leave hospital should be examined by a neurological or medical specialist and ophthalmologist, who will decide whether special reablement in a convalescent home is necessary, and will again, after re-examination, advise by written report on final disposal.

Stiff joints from arthritis, in meningococcal septicæmia, can usually be overcome by physiotherapy.

CHOLERA

Cholera is endemic in many parts of the East and has been known in India since the earliest times. The disease may be spread by human agency from any of these foci in epidemic form. Sporadic cases due to carriers may occur anywhere, but a community under good sanitary control need never fear an extensive spread of cholera. Rogers has shown that cholera does not spread in epidemic form in India if the absolute humidity (the weight of the aqueous vapour in the air measured in terms of its mercury tension) is not above 0 400.

Etiology.—Cholera is caused by the comma-shaped, single-ciliated, gram-negative vibrio of Koch, which lives, multiplies, and produces an endotoxin in the small intestine. Acton and Chopra state that the main actions of the toxic bases of cholera toxin are :—

(1) A fall of blood pressure due to dilatation of the vessels supplying the small intestine, combined with an increased permeability of the vessel endothelium; (2) Direct damage to the secreting tubules of the kidneys which are further hampered by the occurrence of an intertubular œdema as soon as the blood pressure has again risen to normal.

Research work has shown that under war conditions the cholera "carrier" is undoubtedly the most important factor in spreading infection, but the role of water, food, fomites, flies, and faulty conservancy methods must also be kept in mind. Vibrios have been found in the fæces of flies for twenty-four to thirty-six hours after ingestion of infected material by the insects.

Cholera vibrios often disappear from the fæces of patients in three or four days and rarely persist in them for longer than twenty days, but the healthy cholera carrier may go on passing vibrios for a period of two months or longer, a gall-bladder infection having become established. As a rule, however, the carrier excretes vibrios for only a week or ten days. An attack of diarrhœa or the administration of a purgative will often cause vibrios to appear in the stools of a carrier case and a purge may even excite an attack of cholera in a carrier. In India cholera vibrios have been known to live as long as seventeen days in stools kept in the dark with evaporation prevented. The average time of survival is shorter in hot weather—in June one to two days, in February seven days (Greig).

Symptoms.—Incubation period: a few hours to six days or even more. Stages: those of evacuation, algidity, and reaction. In a certain number of cases there is a premonitory diarrhœa, which is probably catarrhal

in nature and may predispose to the choleraic attack. In other cases the *stage of evacuation* commences suddenly with profuse and frequent motions which may or may not be associated with colic. Indeed a sense of relief may accompany the passage of the stool. The attack is usually nocturnal. The motions, at first fæculent and bile-stained, quickly assume the typical rice-water appearance, there being small white flocculi of intestinal epithelium in a slightly opaque fluid. Pints of this material may pour from the patient, who rapidly becomes prostrated. He begins to vomit, and suffers greatly from thirst. The vomited matter, which consists at first of food, soon changes to rice-water fluid, and gushing from the mouth is apt to contaminate attendants. Cramps of the legs and abdomen set in, the tissues shrink, the eyes become sunken, the nose pinched, the skin cold and dusky or earthy in hue, the pulse feebler and the urine less. In the initial stages the brilliant white, pearly colour of the eyelids, especially of the lower lid, makes the eyes appear large and bright. Hiccup may be obstinate and persistent.

livid and bedewed with a clammy sweat. There may be cyanosis, general or localized, and sometimes this is so intense in the lower extremities as to simulate gangrene. The pulse at the wrist may almost vanish, and if a vein is incised only

This concentrated b

has a specific gravit

patient is restless and very thirsty, and may or may not continue to be racked by cramps. While the surface temperature is low that of the rectum is often elevated.

The mind is clear but the patient is apathetic. In fatal cases and usually some ten to twelve hours after the beginning of the attack coma super-

the stage of reaction.

be a bloodshot state of the ey

or severe, and in the latter

During this stage of reaction the patient may die from pneumonia, enteritis, diarrhœa, hyperpyrexia, or uræmic poisoning. Abortive and typhoidal reaction stages are described, and in the latter the pyrexia may last as long as a fortnight.

Such is a picture of cholera gravis, but on the one hand mild ambulant cases occur where the carrier is a special danger, and on the other there is fulminating cholera in which toxæmia causes rapid death before vomiting or diarrhœa have time to set in. Of this nature is the so-called cholera sicca apt to occur amongst debilitated troops. In one of the Balkan wars

rice-water stools were sometimes absent even in severe cases of cholera. It is worthy of note that rashes of various types may occur in cholera, usually during the stage of reaction.

Diagnosis.—It is beyond the scope of this section to deal with the bacteriological diagnosis of cholera, but it is well to remind the medical officer that in suspected carriers who are constipated, rectal swabs should be sent to the nearest laboratory, while in an autopsy on a suspected case of cholera two 5-inch sections of the small intestine, one taken just above he ileocæcal valve and the other from the middle of the ileum, should be ut out after double ligaturing, placed in sterile, well-stoppered bottles id submitted to the bacteriologist as quickly as possible If culture media are available an agar or blood-serum slant should be made from the material at the same time, as the vibrios are apt to be outgrown by the fæcal bacteria.

Differential Diagnosis —Many cases of cholera have been diagnosed as bacillary dysentery, and it must be remembered that the serous form of the latter may closely simulate cholera, amœbic dysentery may sometimes do likewise. It is said that if dysentery coexists with cholera, cramps and rice-water stools may be absent. It should be remembered that dysentery, typhoid, and paratyphoid may coexist with cholera and there may be no sign of the concomitant disease till the cholera is over. There is a form of pernicious malaria which presents choleraic symptoms, but the high axillary temperature should help to distinguish it from cholera.

Severe diarrhœa of the cholera nostras form, food and mushroom poisoning, irritant metallic poisoning, botulism, and the early stages of trichinosis need merely be mentioned. Note that in food poisoning the vomiting usually *precedes* the diarrhœa.

Complications.—Of these gangrene and pneumonia may be mentioned, but remember that intense local cyanosis may be mistaken for gangrene.

Prophylaxis—Personal.—The value of inoculation with cholera vaccine is hard to assess because it is almost impossible to ensure that protected and unprotected groups of individuals are equally exposed to the same risks of infection. But there are strong indications that inoculation with cholera vaccine results in immunity of short duration. The vaccine causes little untoward reaction. Routine anti-cholera inoculation or mass-inoculation in anticipation of an outbreak of the disease are alike unjustified But if an epidemic in civilians reaches the neighbourhood of military units, general inoculation of these units should be carried out. The dosage of vaccine is 0 5 c.cm. followed by 1 c cm. ten days later—a total of 12,000 million organisms being given. In emergency, a single dose of 1 c cm. may be given right off to be followed by 0 5 c cm. when convenient. Extravagant claims have been made for the value of bacteriophage as a protective measure.

The cholera vibrio is extremely susceptible to acid. Therefore the use of lactic acid in tea or the addition of vinegar or 30 drops of dilute hydrochloric acid to every pint of drinking water has been recommended. The last method has been used in India, to all appearance with great success, but some condemn these practices as apt to upset the stomach. Ten-drop doses of eucalyptus oil given twice daily have been strongly recommended

Give in mucilage and syrup of lemons. The vibrio flourishes in an alkaline medium. Long drinks which *dilute the gastric HCl should not be taken*

When possible all indigestible diet should be avoided. Special care is needed as regards fruit, raw vegetables, and meat jellies. Lettuces and celery being moist and eaten uncooked are specially dangerous. Vibrios have been found to survive on lettuce leaves for 29 days. Melons and cucumbers must be avoided, as *they are often perforated and steeped in* water to increase their weight.

Prophylaxis—General.—Cholera patients must be isolated for 42 days [illegible]

cresol solution and allowing it to remain in contact with the stool for at least one hour. Fresh chlorinated lime (1 lb to 4 gallons) may be used in the same way. Roughly, two tablespoons to the pint of cholera dejecta are required. Nothing is better than quicklime if it can be obtained. Add together equal parts of fresh quicklime and water, and then [illegible]

dejecta or vomit, disinfection may be carried out with cresol, or by raking hot ashes over it, or by pouring kerosene over it and setting the kerosene alight. Cholera-soiled clothing, bed linen, and blankets should be stoved [illegible]

possibility—should be kept under surveillance and seen twice daily, morning and evening, for five days.

Carriers should be sought for, particularly among those handling food *in any way and those suffering from diarrhœa. When found they should* be quarantined until the stools are negative, usually for three to four weeks. As regards carriers, it must be remembered that use of purgatives may induce an attack of cholera.

Control of food and drink is of the utmost importance. Cholera is *very often water-borne* and all drinking-water as well as all water used for washing and bathing should be carefully chlorinated. If this is not possible, drinking water at all events must be boiled. Wells and other water-sources *and bathing places of all kinds must be policed and properly* supervised, and put out of bounds if necessary.

Water bottles should be disinfected with boiling water, strong bleach solution, or potassium permanganate. The latter is also used for the *disinfection of wells and for other purposes*, because it has a special *destructive action on the vibrio of cholera.*

Ghurras, water chatties, and massacks are often the source of infected water. Most careful supervision is required of mineral waters, ice supplies and the like.

As regards food-supplies, all milk should be boiled and dairy products *of all kinds obtained only from reliable sources.* Avoid uncooked vegetables and fruit that is eaten unpeeled.

Anti-fly measures of all kinds should be carefully carried out and particular attention paid to the protection of food against flies (*see* Arthropod Pests and Appendix I).

Dish-cloths and cooking-utensils should be boiled and special attention paid to the cleanliness of cookhouses.

Latrines should be properly disinfected, especially if fly-proofing is not satisfactory

Finally the importance of mild and ambulant cases must be appreciated and a careful search made for these. In particular the stools of all those within units who are suffering from diarrhœa, including followers and employed labour, must be examined for the presence of *Vibrio choleræ*.

Treatment.—For the most part drugs are of little use in cholera. The Indian practice is to treat the premonitory diarrhœa by giving half an ounce of castor oil with a tea-spoonful of brandy. This is probably wise, as it clears the bowel of irritating material

Even in the mildest cases absolute rest in bed is essential, a warmed bedpan being provided. No food other than glucose is to be given while the disease is active. The surface of the body must be kept warm. Hot sandbags to the body are useful and so is kneading of the muscles to relieve the intolerable cramps. But intravenous saline is the best treatment for this symptom

Ice and a small hypodermic of morphine may check the vomiting—if, indeed, opium in any form is justifiable in cholera—but it must be remembered when giving drugs subcutaneously in cholera that they remain unabsorbed during the algid stage, and when the reaction sets in the drug or drugs which have been injected may be taken up in quantities which prove poisonous.

Fluid should be given in sips, as large drinks are apt to excite emesis Stimulants may be necessary Coramine is useful. Hot tea and black coffee have been recommended.

Native aluminium silicate (kaolin) is claimed to be a specific both for cholera and for acute bacillary dysentery. The method advocated is as follows To 250 c.cm. of cold boiled water add 100 grammes of kaolin pulverized and shaken until the mixture has become creamy and homogeneous. Give a tumblerful every half-hour, or hour, to six or more doses. Smaller doses are continued over several days. If the patient is too ill to swallow, the mixture should be given by means of a stomach tube.

The standard treatment for cholera, ho[illegible] that of Rogers. It [illegible]

duced at the rate of not more than 4 ounces a minute.

Where there is a doubt as to the necessity for the employment of his method, Rogers estimates the specific gravity of the blood. As full particulars are given in the booklet accompanying the cholera equipment nothing further need be said regarding the method here. It seems,

however, convenient to tabulate his latest summary of the procedure he *now follows* :—

1. On admission 1/100th grain atrophine sulphate and repeat *night* and morning.
2. Take specific gravity of blood, blood pressure, and oral and rectal temperatures.
3. If blood pressure not over 70 mm. or specific gravity is 1,063 or over, inject *3* to *6* pints of fluid according as specific gravity is 1,063-4-5-6 in adult males. Less for females and children.

   The *first pint consists of the alkaline solution mentioned in para* 8, the remainder is hypertonic saline; thus, if 4 pints are indicated, give 1 of the alkaline solution and 3 of the hypertonic, continued through the same flask and cannula.
4. Unless rectal temperature is below 99° F. saline should never be injected at above 98° F. Risk of hyperpyrexia.
5. If rectal temperature is 100° F. or over, give hypertonic solution at temperature between 80° and 90° F.
6. Normal saline, *i.e.* 90 grains NaCl, 1 pint every two hours by rectum till collapse stage past and urination re-established. Then every four hours until 2 pints urine in twenty-four hours.

   If the urine is acid give the alkaline solution mentioned in para. 8 instead of normal saline.
7. Fall of blood pressure to 70 mm. and under, or rise of specific gravity to 1,063 or above, are indications to repeat injections morning and evening and at any time when pulse fails or patient restless.
8. At each intravenous injection, give 1 pint of sodium chloride 90 grains and sodium bicarbonate 160 grains (2 per cent.) (*See* para 3.)

   N B.—Sterilize the sodium bicarbonate in paper in autoclave and add to sterile salt solution.
9. Repeat alkaline injection later if urine deficient and blood pressure *100 mm. or more and specific gravity* below 1,063. (Normal for Europeans = 1,058; for Indians = 1,056.)
10. If blood pressure remains persistently much below 100 mm. and urine is deficient, give pituitary extract and caffeine sodium salicylate (5 grains by mouth every four hours). Cup and foment over kidneys.

[illegible] be pro-

[illegible]

principles advocated by Sir Leonard Rogers are [illegible] h some minor modifications. No provision is made for the estimation of the specific gravity *of the blood; instead, reliance is placed on* blood pressure estimations and five modern mercurial sphygmomanometers are provided for this purpose in each unit.

It should be here noted that while *there is no question* as to the urgent necessity of fluid, introduced by the quickest possible route, in cholera, it *is questionable if hypertonic* saline and alkali solutions have any marked

advantage over normal saline solution which is simpler to make up and can often be prepared and administered more rapidly than the above-mentioned more complicated solutions. In most cases the general appearance of the patient with his very evident intense dehydration is sufficient indication for an immediate intravenous saline injection, and 4–6 pints may be given immediately in such cases without wasting time in estimating the blood pressure, etc. The general guiding principle should be that if time permits the rigid technique advocated by Rogers (with certain modifications mentioned in the pamphlet accompanying the cholera unit) should be followed. In very urgent cases or where facilities do not exist for the full technique, the simplified technique outlined above may be used.

If rigor follows transfusion use hot bottles temporarily till it is over Collapsed cases after the rigor may benefit from ¼ grain each of morphine and belladonna extract, but, as stated, opium must always be used with care in cholera.

The other part of Rogers's treatment consists in the administration of calcium permanganate water from 1 to 6 grains to a pint, and 2-grain coated potassium permanganate pills given very frequently at first. Details will be found in the equipment booklet Continue the pills until the stools become green and less copious Along with the permanganate 10 minims of a 1/1,000 solution of adrenaline chloride may be given every three hours to re-establish the urinary secretion Keep the patient warm and apply turpentine stupes to the abdomen Serum therapy in cholera is still on its trial but promises well. The dose is 40–100 c.cm. intravenously.

The administration of solutions of glucose has been strongly advocated, either a 10 per cent. solution intravenously or an isotonic solution (4½ per cent) subcutaneously. In view of the results obtained in pneumonia it may be advisable to employ hypertonic glucose (25 per cent) intravenously. Distilled water should be employed as the solvent, not normal saline.

Lately an old-time remedy for cholera has been revived, with encouraging results. This is a mixture of essential oils given in the following formula :—

Spt. aether.	min. 30
Ol. cajuput.	
Ol. cloves	
Ol. juniper	aa min 5
Ac sulph. arom.	min. 15

Dose.—One drachm, in half an ounce of water, every half-hour until vomiting and purging cease. The same dose is administered to contacts once or twice daily for one or two days

A useful mixture for the reaction stage is as follows —

Bismuth. salicylat.	gr. 15
Sod. bicarb	gr. 5
Liq. opii sedativ.	min. 5
Mucilaginis	q.s.
Aq. chloroformi ad	1 oz.

At this stage, also, if the diarrhœa is troublesome rectal injections of tannin, 1 ounce, gum arabic, 1 ounce, and warm water, 1 quart, are indicated.

Inquire as to retention of urine and treat anuria by poulticing or dry cupping over the kidneys.

At a later period alkalies and digitalis will be found useful. A serious symptom to be promptly combated is the occurrence of coma. As there is marked acidosis in cholera, the method of giving 3 per cent. sodium bicarbonate solution by subcutaneous injection seems reasonable. It may be given frequently in quantities up to one litre, if not already employed during transfusion.

The diet for convalescent patients must be very bland and easily digested and the return to ordinary diet carefully regulated.

Much work has been done on both the prophylaxis and treatment of cholera with bacteriophage The results are, up to the present, inconclusive. Sulphonamides have been used but it cannot be said that their effectiveness is proved. None the less, they are worth giving as for bacillary dysentery.

CYSTICERCOSIS*

Cysticercosis is the term given to the somatic infestation of man by cysticercus cellulosæ, the larval or bladder-worm stage of the tape-worm, *Tænia solium*.

There is no authentic record of the infestation of man by cysticercus bovis, the corresponding stage of *T. saginata*, the common tape-worm of this country.

The adult tape-worm, *T. solium*, is a parasite of man alone and normally the larval stage is passed in swine, the parasitized flesh being known as "measly pork".

Formerly cysticercosis was common in Europe, more especially in Germany, where uncooked ham was popular. Of late years the disease has become a rarity in this country and practitioners have tended to forget its potentialities; and it is only comparatively recently that cysticercosis has been recognized as a common cause of a form of epilepsy developing *de novo* in British soldiers returning from service in the East, especially from India.

Etiology.—Since each gravid segment of T. solium contains some 40,000 [illegible]

through the agency of flies. The human host of the adult [illegible] contaminate his hands and thence his food with eggs passed by himself and thus suffer auto-infestation and, it has been suggested, another form

* Abridged from the chapter by MacArthur on Cysticercosis in the "British Encyclopedia of Medical Practice", Vol. 3.

of auto-infestation may occur by the regurgitation of gravid segments from the gut into the stomach. By whatever path the eggs are introduced into the alimentary tract of man their subsequent development resembles that which takes place in their normal host, the pig. The liberated embryos with the aid of their tiny hooklets penetrate the intestinal mucosa and are borne by the blood stream to their final habitat which, in man, is usually the brain and voluntary muscles Any tissue or organ may, however, be affected As regards the brain, the grey matter is invaded more commonly than the white. The parasite may also invade the eye and may occasionally be seen moving in the anterior or posterior chamber of that organ

The total infestation may vary within the widest limits, from one single cysticercus to many hundreds; infestation may be limited to one organ such as the brain, or be generalized throughout the body.

The morphological development of the cysticercus is completed within three or four months of entry Except in the brain the cysticerci become walled off by a clear-cut fibrous capsule, the host capsule, the effect of which is to protect both the parasite and the host. In the brain encapsulation to a lesser degree results from the proliferation of surrounding neuroglial tissue together with cellular reaction In most cases, as long as the parasite remains *alive*, a relative equilibrium appears to be attained between the encapsuled living cysticercus and the host tissues, both continuing to live in a state of symbiosis When, however, the cysticercus dies, it acts as an irritant foreign body, liberates toxic products while undergoing degeneration, and exerts increasing pressure on the surrounding tissues through the progressive distension of the cyst capsule by fluid. A further cellular reaction is now provoked and damage to the cyst wall allows widespread penetration of the toxic products of disintegration

This brief description of the morphology of the cysticercus especially when it infests the brain, may help to explain some at least of the puzzling neurological symptoms connected with its presence in this organ, and why it is that parasites may be lodged in the brain for a term of years (at least six) before they begin to give rise to symptoms, and why these symptoms, when present, may wax and wane in intensity and alter both in character and localization, sometimes in a most dramatic and kaleidoscopic manner

The duration of life of individual cysticerci varies within wide limits, as a rule they die off gradually so that dead calcified cysts and living parasites may co-exist in the same individual and even the same organ Many parasites die off between the third and sixth years, though viability for a much longer period is possible. The deposition of sufficient lime salts to cause a shadow in a radiograph takes at least three years from the time of death of the parasite, and those cysts which parasitize the brain show relatively much less tendency to calcify than those occurring elsewhere.

Symptoms —In some cases, infestation of the brain with cysticerci s so overwhelming that the host is unable to withstand the onslaught and dies during the early stage of infestation and development of the larval cysticerci In these fulminating cases death may result within a week of the onset of symptoms, the clinical picture resembling that of an acute encephalitis; or the patient may develop signs of increasing intracranial

pressure, leading to coma and death within a few months. In attacks such as these, which are exceptional and consequent on overwhelming infestation, the most characteristic signs of cysticercosis, palpable subcuticular cysts and major epileptiform attacks, may not occur, since they have not had time to develop.

Normally, three clinical stages, with a certain degree of overlap between them, may be recognized. These are :—

(1) The incubation period.

(2) Period of premonitory symptoms.

(3) The established disease.

Incubation Period.—This is the interval between the original infestation and the onset of symptoms. It is usually difficult, for obvious reasons, to establish even approximately when the original infestation took place. Even if the patient was known to have been harbouring an adult tapeworm and therefore passing gravid segments containing eggs from any

within two years of proceeding to an endemic area.

Premonitory Symptoms.—These occur during the active life and development of the parasite. The symptoms occurring at this stage ... to be recognizable in retrospect when

during this phase. In many cases there is a complete absence of such premonitory symptoms, the first evidence of the disease being an epileptic fit or the finding of palpable subcuticular cysts.

Established Disease.—The most objective symptom of this, the final stage, is the finding of one or more palpable subcuticular cysts. The number and positions of these cysts vary greatly from patient to patient and from time to time in the same patient. Cysts, which have been in evidence maybe for years in one site, may collapse and disappear within a few days, while other cysts may become palpable in sites where previously they could not be detected. This late appearance of cysts, in some cases spread over a dozen or more years, occurs through the distension of the cyst capsule with fluid, this being associated with the death of the contained parasite. The appearance and disappearance of these palpable swellings may lead the patient to imagine that his "little lumps" have the power to migrate from place to place.

... about the size of a small

sufficient size and prominence they can often be seen as well as felt, more easily in some sites (*e g.* forehead) than in others. They are more commonly found in the upper half of the body than the lower owing to the smaller muscular development and less cover for the cysts in the former.

The size and shape of the individual cysts vary with their age and site. In the brain, where they meet an equal resistance on all sides, they tend to be globular and average about a centimetre in diameter, those lying between muscle fibres and separating them are oat-shaped and may attain a length of two centimetres when fully grown The subcutaneous cysts are usually symptomless and one has to look and feel for them as they are seldom complained of. Palpable cysts are not a necessary feature of cysticercosis and the brain may be studded with cysts without any being found elsewhere.

Epileptic attacks constitute the most important presenting symptom of brain infestation and usually develop only when the cysticerci have been present for several years The epileptic seizures may vary greatly in character. In some they resemble major epileptic attacks so closely that patients have been kept under treatment for so-called idiopathic epilepsy for many years before the true etiology of the condition has been recognized. Other attacks may resemble petit mal, or the patient may have a series of Jacksonian attacks, a feature of which may be that each attack starts in a different group of muscles. The fully developed epileptic seizures or Jacksonian attacks may be preceded for months or years by "larval" attacks consisting of localized muscular spasms which may possibly have been regarded as a hysterical manifestation The onset of the first epileptic attack may coincide with the appearance of the first subcutaneous cyst, or cysts may have made their appearance for a long time—up to six years—before the first fit is registered, on the other hand, the brain symptoms may precede the advent of palpable cysts by months or years. Epilepsy is by no means the only evidence of cerebral involvement and a wide range of symptoms may occur referable to the area or areas of brain attacked. Syndromes closely resembling hysteria, insular sclerosis, neurasthenia, and various psychoses may occur with or without epileptiform seizures. Indefinite temperamental changes similar to those following epidemic encephalitis may also occur. Whatever form the brain symptoms may take epileptiform seizures or Jacksonian attacks are usually met with at some stage of the disease

Prognosis.—Prognosis of individual cases is very difficult and must be extremely guarded Dixon and Hargreaves, who carefully followed 284 cases, are able to say that the general outlook for the average case is certainly brighter than MacArthur first supposed Some infected persons may never have any symptoms of the disease, some have only minor cerebral symptoms, but others have persistent major epileptiform convulsions and other serious manifestations, such as marked papilloedema Symptoms come on at varying periods after infestation, from several months to more than ten years

In Dixon and Hargreaves's series, mortality was 8 per cent. and they noted improvement in patients whose outlook had seemed hopeless for some years. They were unable to confirm the belief that between the sixth and eighth year after infection was a particularly dangerous time, in fact, of the patients whose symptoms were of from five to ten years' duration, 45 per cent were improving and 8 per cent. had become symptom-free for three years or more. Of their patients still alive, 92 per

cent. were either unchanged, improving, or free from symptoms; among these, 36 per cent. were showing improvement and a further 15 per cent. had been free from symptoms for at least three years.

Despite this more cheerful outlook for the group as a whole, Hargreaves and Dixon emphasize, with MacArthur, the difficulty of prognosis in individual cases. A great variety of clinical syndromes may result from cysticercosis, among these may be mentioned status epilepticus, progressive dementia, and asthenia, maniacal outbursts which may necessitate residence in a mental hospital, symptoms paralytic or otherwise suggestive of an advancing cerebral tumour or of increasing intracranial pressure, etc., etc.

Diagnosis.—One of the most important factors in the diagnosis of cysticercosis is the awareness of the possibility of its occurrence, especially in individuals who suddenly develop epileptic seizures during healthy adolescent or adult life, particularly if they have served in India or in other stations where infestations with *Tænia solium* are common. This diagnosis is all the more likely to be correct if there is no previous personal or family neuropathic history.

It must be remembered that cerebral cysticercosis may simulate very closely both idiopathic epilepsy and cerebral tumour and in the absence of palpable cysts or of radiological evidence it may be impossible to distinguish them.

The positive diagnosis of cysticercosis depends on one or both of two objective findings. These are —

(1) The presence of palpable cysts.

(2) Calcification of cysts containing dead parasites.

It must be emphasized that unless the cysts are very superficial they are not palpable before the death of the parasite, palpable cysts being therefore in most cases a relatively late manifestation. Calcification of the cyst is a still later phenomenon and usually at least three years elapse after the death of the parasite before sufficient calcium has been deposited to be seen in a radiograph, and, as mentioned previously, calcification of intra-cerebral cysts is relatively rare at any stage.

The patient under suspicion should be carefully examined for palpable cysts from top to toe, the muscles being rolled and kneaded under the hands whilst alternately contracted and relaxed. He should be carefully questioned whether he has noticed any small lumps at any time and should be warned to look out for their future appearance.

To demonstrate the parasite a suitable cyst is excised under local anæsthesia and examined under the microscope. The hooklets on the scolex are diagnostic and characteristic.

The radiological examination of the patient for calcified cysts is also very important and an exact technique must be carefully followed. The following regions are radiographed :—skull, lateral view only; root of neck, upper arms, fore-arms; thighs, legs. The films and intensifying screens should be free from blemish, and note should be made of any blemish on the patient's skin such as tattoo marks. The exposure aimed at should be suitable for bone detail with a slight under-exposure. Exposures suitable to demonstrate soft structures may mislead. Shadows

vary from a small and easily missed "dot" less than a millimetre in diameter, signifying a calcified scolex, to a fully grown elliptical cyst more than two centimetres long The search throughout the soft tissues must be very thorough. If no calcified cysts can be seen after a thorough search another series should be taken and examined in a year's time, and so on, year after year, as long as the diagnosis remains still in doubt. It must be emphasized that calcified cysts in the brain are rare and must never be expected, although, of course, they must be looked for. (Plates 10–11)

The calcified cysticerci can hardly be confused with the calcified encysted larvæ of *Trichinella spiralis*, which also parasitize human muscle. The latter are minute and can hardly be seen without a magnifying glass.

A blood count gives little assistance in diagnosis. An eosinophilia may be present during the invasion stage and later when the cysts are degenerating. The cerebro-spinal fluid is but little affected though there may be considerable increase of pressure with a moderate lymphocytosis

Complement fixation tests, using an alcoholic extract of *Tænia* species as antigen, have proved useful in some cases, although on the whole disappointing

Cases suspected of suffering from cysticercosis should be kept under observation and thoroughly investigated at regular intervals, a series of radiographs being taken at intervals of one to two years

Treatment.—Treatment is unfortunately, at the best, only palliative. Phenobarbitone and the bromides are often useful in controlling the fits From a consideration of the essential pathology of the disease it can be assumed that any larvicide is contra-indicated unless it can be made effective at a very early stage of the infestation.

Theoretically, at all events, we should rather look for an elixer which would enable the larvæ to continue to live in symbiosis with their host to a mutual old age Surgery, except as an emergency measure, has little scope in the treatment of cysticercosis and is only justified in those cases in which life or some important function is directly threatened Relief from such interference is usually only temporary.

Prophylaxis—Since there is no treatment for the established disease its prevention is of the greatest importance Essential points are as follows —

1. Personal hygiene must be of high standard, hands should be washed before and after meals and after defæcation
2. Latrines must be satisfactory so that ground is not fouled
3. Drinking water must be remembered as a possible source of infestation. Chlorination will not make it safe in this respect, but filtration or boiling will do so.
4. Vegetables must be avoided in the tropics unless they have been cooked.
5. Pork must be well cooked to kill larvæ and should not be accepted unless it comes from pig farms and abbatoirs that are su[illegible]
with great thoroughness.

DENGUE

Dengue occurs chiefly in the tropics, but also extends into sub-tropical areas and as far beyond this as the vector is found. It is most common along littorals, probably because the mosquito *Aedes (Stegomyia) ægypti* is usually numerous in sea coast places. The disease tends to cause sharp, explosive epidemics, and many pandemic outbreaks have been recorded, these often occurring at about 20-year intervals.

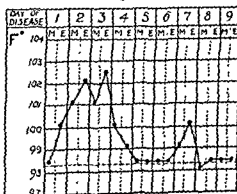
Etiology.—The chief vector of the disease is *Aedes ægypti*, as proved by experimental research in Australia, where it has been shown that the blood of patients suffering from an attack of dengue can reproduce the disease when inoculated subcutaneously into healthy persons, and that infected *Aedes ægypti* transported to a dengue-free locality can cause the disease by their bites. It is due to a virus which is present on the second and third day in the patient's blood, possibly it may persist for a longer period.

In New Guinea *Aedes scutellaris* has been proved a vector.

Other probable carriers are *Aedes albopictus* and *Armigeres obturbans*: the evidence regarding *Culex fatigans* is conflicting, and all recent work has failed to confirm the earlier opinion regarding the responsibility of this mosquito in the spread of dengue.

Symptoms.—Incubation is five to nine-and-a-half days according to the Australian work, but in all probability it may be shorter or longer. Onset very sudden, with rapid rise of temperature, which may reach 105° F.

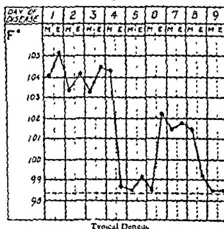
Fig. 29.



Temperature in mild case of Dengue.

itching of the palms and soles may occur at the same time. Very soon the patient is suffering from severe headache, chiefly supra- and post-orbital, and the typical joint pains, which are really located in the tendinous insertions about the joints. There is also myalgia, most severe in the back. The condition indeed closely resembles that met with in influenza, but, as a rule, coryzal signs are absent. The ocular muscles are specially affected, and every movement of the eyes causes pain. The pulse is slightly accelerated but soon slows. This slowing of the pulse with high fever (Faget's sign) has been very characteristic of recent epidemics of dengue. In this respect, as in some others (e.g. transmission by *A. aegypti* and length of incubation period) dengue resembles yellow fever, especially those comparatively mild cases without jaundice. Swollen glands may make their appearance. Insomnia is present and there is severe mental and physical depression, while malaise and anorexia are

Fig 30.



Typical Dengue

marked. A feeling of giddiness is common. Constipation is the rule at the outset. There is no albuminuria. The temperature remains high for three or four days, then drops, it may be, to normal, continues low for twelve hours to three days, and then rises again sharply (Figs. 29 and 30). During the interval, which may be absent altogether, the patient feels better, but, with the relapse, the pains and other general symptoms start again. This stage, however, is short, but is marked by the appearance of the terminal rash, and may be signalized by a regular crisis with sweating, diarrhœa or epistaxis. Sometimes a crisis of this kind accompanies the first fall of temperature. The true dengue rash resembles that of measles, begins about the bases of the thumbs and the back of the wrists and soon appears about the big toe and ankle. Then the elbows and knees may be involved, and sometimes the exanthem spreads all over the body. The palms and soles may take on a carmine flush. F-

mation follows when the rash has been pronounced. This second stage may be very brief, or may last for a couple of days.

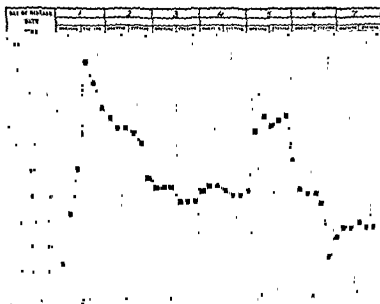
The disease is very rarely fatal, and then nearly always owing to complications.

Convalescence is apt to be slow and marked by neurasthenic symptoms such as mental irritability or depression.

Leucopenia and reduction in the polymorphs constitute the most marked blood changes. There is also an increase of lymphocytes and a late eosinophilia. Eosinophilia is recorded most frequently in localities where helminthic infections are common, and possibly may merely indicate a return of the blood to its pre-febrile condition.

While the above symptoms are those of typical dengue, it must be

Fig. 31.



Saddle-back Temperature in case of Seven-day Fever—Typical Dengue

remembered that these are so-called six- and seven-day fevers which, for all practical purposes, may be classed as dengue. *In these the typical* [illegible]

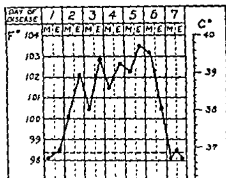
[illegible]

Philippines show that dengue may be so mild in its manifestations as to be unrecognizable with certainty except by transmission experiments, and that an infected person may even remain afebrile throughout and yet be capable of infecting mosquitoes. *Dengue* is usually a mild though debilitating disease, but severe epidemics or pandemics appear from time to time, especially in non- or only mildly-endemic areas of the disease.

In the severe Athens epidemic of 1928, gastro-enteritis, vomiting, and hæmorrhages into the skin and mucous membranes, were among the many symptoms reported. Immunity after attack is very variable in degree.

Differential Diagnosis.—It must be differentiated especially from influenza, yellow fever, and phlebotomus (sandfly) fever, and to a less extent from malaria, early enteric or paratyphoid, scarlatina, measles, early smallpox, and rheumatism. Mild infections due to *Leptospira icterohæmorrhagiæ*, and to allied species or strains, may have a close resemblance to dengue, but differ in that albuminuria seems to be a constant feature Rift-Valley fever, first described in Kenya Colony in 1931, resembles dengue in many respects. This disease, which occurs from time to time as a fatal epizootic amongst ewes and lambs, also attacks those in close

Fig. 32.



Atypical Dengue simulating Early Typhoid or Paratyphoid

contact with them, such as shepherds and laboratory workers The causal organism is a virus and is supposed to be transmitted by a mosquito, *Tæniorhynchus brevipalpis*.

The almost invariable respiratory involvement in influenza is a distinguishing character, while the rash of dengue is absent in influenza

In yellow fever albumin will be found in the urine at an early date

Blood inoculation intracerebrally into mice causes no symptoms, thus differentiating dengue from yellow fever and Rift-Valley fever

Although typical dengue is easily distinguishable from typical sandfly fever on account of the longer course, relative severity, and secondary rash, usually met with in the former, atypical attacks of either may be impossible to differentiate on clinical grounds alone

Indeed, some declare the two diseases to be identical, and we are led to ask if the same disease in altered form may not be transmitted by totally different insect vectors.

For the present it is clearly advisable to consider dengue and phlebotomus fevers as separate and distinct diseases and to allot a section of these Memoranda to each of them; admitting, however, that, in many

cases, the short form of dengue is clinically indistinguishable from sandfly fever.

The onset of dengue is different from that of malaria, but may resemble the early stage of typhoid and paratyphoid (*see* Fig. 32). Careful observation should, however, serve to distinguish dengue from these fevers and from the other diseases mentioned above.

Prophylaxis.—*Destroy domestic mosquito-breeding places and protect from mosquito bites by adoption of all the measures of which full details are given in the section dealing with mosquito control (see* Arthropod *pests and Appendix I).*

Treatment.—Light diet. Phenacetin and aspirin relieve the pain and headache. Morphine is rarely necessary and is better avoided. Cold spongings are useful, especially for insomnia.

During convalescence, if there is much depression, a sound wine may be ordered.

DIARRHŒA

Acute diarrhœa unconnected with any specific infection or disease is often encountered in the East. Commonly ascribed causes are exposure to chill and irritation of the bowel by sand and dust or by coarse and unsuitable food. Diarrhœa due to the last-named cause was prevalent among African troops and followers during the war of 1914-18, and in [illegible]

and the possibility of dysentery, bacterial food-poisoning, and cholera carefully excluded by the appropriate examinations.

Prophylaxis.—*Chilling of the abdomen must be avoided, particularly* [illegible]

taining sand, mica, or excessive amounts of organic matter may cause diarrhœal outbreaks and must be appropriately treated to remove these. In all other respects the prevention of diarrhœa should follow the general lines laid down for the prophylaxis of bacillary dysentery (p. 111).

Treatment.—In countries where dysentery is prevalent it is advisable to treat every case of diarrhœa from the start as potential bacillary dysentery and to administer a sulphonamide at once—preferably sulphaguanidine because it is slowly absorbed and has been proved relatively safe for out-patient treatment. Succinyl sulphathiazole, sulphadiazine, sulphanila- [illegible] results in the hands of [illegible] ly given [illegible] g. and maintenance doses of 2–3 g. usually effecting a speedy cure, which suggests that many of these so-called non-specific diarrhœal attacks are, in fact, of dysenteric origin.

When catharsis is exhausting, or griping very severe, a hypodermic

injection of morphine and atropine may be given, but is better avoided unless necessary. Remember that cholera may commence, especially in Europeans, with a preliminary stage of diarrhœa, and that in this disease opium is hurtful, except, according to some authorities, at the outset.

Apply heat to the abdomen. A hot bath, when it can be managed, sometimes acts like a charm, and in diarrhœa due to chill and exposure even bathing the feet and legs in hot water and mustard does good.

After the period of starvation has been completed, give hot milk diluted at first (one part to four parts of rice-water), Benger's food, or gruel of any kind, and gradually work up to a normal diet.

Acute Gastro-Enteritis in Children

This is often a manifestation of infection with one or other of the dysentery bacilli. Whatever the cause may prove to be, do not wait for a laboratory diagnosis but commence treatment without delay. Remember that malaria may be a cause of diarrhœa.

Treatment.—Sulphaguanidine, or some other sulphonamide, should be given as for the treatment of bacillary dysentery, if the diarrhœa is or may be due to that disease. (*See* section on Diarrhœa.)

The following, in the main, is the treatment advocated by Green-Armytage.

Indications.—(1) Get rid of the poison, and so allow the inflamed intestine to recover. (2) Counteract acidosis. (3) Supply the fluid lost —dehydration is the common cause of death. (4) Provide a proper diet.

These indications, in the sequence given, may be met as under —

(1) Half-hourly, or hourly, doses of

Sod. sulph.	gr. 20
Sod. bicarb.	gr. 10
Sod. cit.	gr. 10
Glycerin.	min. 20
Aq. anisi	1 drachm

until stools become watery and brown.

If there is vomiting, wash out the stomach with 1 per cent. sod. bicarb. given through a catheter and funnel. If the vomiting is very severe, give gr. $\frac{1}{10}$ of calomel every hour for six or eight doses. One-minim doses of tinct chlorof. et morph. co. are often useful.

(2) Half-a-teaspoonful of sod. bicarb. and half-a-teaspoonful of common salt to one pint of boiled water, add gr. ½ of saccharine to make palatable. The child is encouraged to take as much of this as possible The salt makes it thirsty and so it drinks more readily. If œdema is present, give the drink without salt.

Raisin tea —One tablespoonful of white raisins to one pint of boiling water, crush and strain. Infants and small children readily take one ounce, or more, an hour.

(3) In mild and early cases, the alkaline solution given under (2) suffices. Infants will take two pints in twenty-four hours almost continuously if given through an easy teat.

In late and severe cases, 4–6 ounces of saline given under the skin of the axilla every five hours. If the child is extremely ill, give the saline intraperitoneally—pick up the abdominal wall just below the umbilicus, pass in a large Record-syringe needle at right angles for 10 inches, release hold on abdomen, and inject a pint of saline.

(4) Nothing but rice-water prepared as follows:—One tablespoonful of rice to 1½ pints of water, boil, strain, add a pinch of salt and a teaspoonful of brandy.

After forty-eight hours, give whey, or skim milk diluted 1 in 3.

Instead of subcutaneous injections of saline, 5 per cent. glucose may be given combined with injections of insulin.

If there is reason to believe that an attack is of dysenteric origin, shiga antitoxin should be given in a dose of 20,000–50,000 units subcutaneously.

DYSENTERY

Dysentery is a term denoting a symptom complex, namely the passage of blood and mucus from the bowel, and may be due to various pathogenic agents.

From earliest times dysentery has been, beyond others, the disease of armies in the field; during the war of 1914–18 it was the most common medical cause of inefficiency. Not only so, but it was responsible for many deaths, and left many men more or less permanently disabled.

Despite statements to the contrary, it may be confidently asserted that in each of the war areas the bacillary type was more prevalent than the amœbic. Indeed, it would seem that *epidemic* dysentery, with a few notable exceptions (*e g.* the Chicago epidemic), is always of the bacillary type. The amœbic form, however, was present in many war areas, more especially in Burma and East Africa. Indeed, where Indian and native African troops are employed it is probable that much more amœbic dysentery occurs than in areas where only European troops operate. In careful surveys only about 5–10 per cent. of the dysentery cases were amœbic.

Dysentery caused by two intestinal protozoa, the flagellate *Giardia lamblia* and the ciliate *Balantidium coli*, by the malarial parasite *P. falciparum*, and by the trematode worm *Schistosoma mansoni*, are forms which must not be forgotten. There are also other causes of dysentery, such as ulcerative colitis of unknown origin, but these need not be discussed here.

Much is heard of "flagellate dysentery," and the evidence of possible pathogenicity is strongest as regards *G. lamblia*, but in some instances a low degree of infection with *Entamœba histolytica* is overlooked because of the large numbers of *Giardia* present in the stools. As Dobell forcibly says, "Often we read that some intestinal flagellate was the 'cause' of a patient's intestinal disorder because 'no other cause could be found.' The absurdity of such statements is obvious. If such reasoning were permissible, one would have to suppose that many cases of diarrhœa, in which neither flagellates nor other organisms can be found, are due to no cause at all."

Note.—With a view to prompt and ... importance to ... of dysente... such facilit...

AMŒBIASIS

Entamœba histolytica is responsible for lesions other than dysentery. The lesions due to this organism, wherever they occur, are grouped under the general heading *Amœbiasis*

Intestinal Amœbiasis (Amœbic Dysentery)

The cause is *Entamœba histolytica* *E. coli* and the other entamœbæ shown in Fig 33 and so frequently found in the stools are non-pathogenic. The differences between both the vegetative and cystic forms of three of these entamœbæ are also shown in the figure The important point for the clinician and sanitarian to remember is that the vegetative forms of the dysentery amœba, *i.e.*, those which throw out pseudopodia, absorb nourishment, and manufacture toxins, are not resistant outside th... They easily perish, but this is not true of th... are in contact ... capable of ... semi-solid ... dysenteric patient, whether co... good health, is the carrier and the principal danger in camp life. Apart from the carrier, infection may take place through the medium of water, uncooked moist food, flies, wind, soiled toilet-paper blown from open latrines, and possibly also from dust, if the cysts have not had time to dry and perish It has been definitely shown that house flies, and some other allied species, take up living cysts from infected stools and transmit them in their excreta to food or drink.

When the cysts are swallowed by man they pass through the stomach and excyst in the intestine The liberated amœbæ are pathogenic and establish themselves in the large intestine.

The incubation period in amœbic dysentery is variable, often over 60 days but occasionally much shorter—the incubation period was stated to be under a week in some instances in the Chicago outbreak. In bacillary dysentery it is usually less than a week.

Amœbic dysentery occurs as an endemic or sporadic infection, and our knowledge regarding it and its cause is still defective. For example, it has been shown that a considerable number of apparently healthy people who have never been out of England, where amœbic dysentery is not generally recognized as endemic, may harbour *E. histolytica* Hence it would seem that it is only under certain conditions, of which we are as yet ignorant, that this protozoon manifests itself as a pathogenic agent.

Some authorities believe that man may be attacked by two strains of *E. histolytica* One, a large strain, is highly pathogenic and highly invasive, the other, a small strain, is only very mildly pathogenic with low invasive powers. This hypothesis of two strains or races, differing markedly in pathogenicity and invasive power, fits in with many of the observed facts connected with this baffling disease.

Symptoms.—Two chief types of amœbic dysentery may be distinguished one with an insidious onset commencing with diarrhœa and without much general disturbance, the other more acute with severe griping. In the former, three or four pultaceous stools may at first be passed in the day and there is often tenderness over the cæcum and along the line of the large intestine. Very acute attacks are rare. The onset as a rule is much more gradual than in bacillary dysentery.

Dysentery is more common in the subacute form which, after premonitory diarrhœa, starts with griping pain in the right and left iliac fossæ, often severe, and the frequent passage of motions containing blood and mucus, such passage being associated with much straining and, if the rectum is involved, tenesmus. Usually, when the disease is established, there are about ten to fifteen in the twenty-four hours. At the start they may contain merely dark fluid blood and mucus. The latter is not so sticky, nor is the blood so bright as in bacillary dysentery. The stools have a foul odour. Later, when ulceration has proceeded apace and the blood is decomposing, the appearance of the stools has been aptly likened to anchovy sauce.

Solid stools coated with clotted blood and mucus may be passed at periods when the condition is quiescent.

As a rule there is no fever, but nausea and vomiting often occur, the ... The disease tends to

supervene. The hæmorrhage may cause death, the gangrene may result in fatal perforation, or mere exhaustion may kill the patient. Hepatitis and liver abscess are a not infrequent complication and should always be kept in mind.

... may be present. Very often this chronic course is punctuated by exacerbations, when there is abdominal pain and some tenesmus. Gangrene may supervene and sloughs be passed.

... special mention, for it is

stools examined for amœbæ.

Morbid Anatomy.—The ulcerative process, brought about chiefly by the ... down to the submucosa and elaborating their toxins, ... ture, and sigmoid ... e rectum may be ... he small intestine.

The condition found *post mortem* varies from nodules of infiltration surrounded by a red ring of dilated vessels to large circular or oval ulcers with undermined edges, the latter having the longer diameter, lying as a rule, transversely They have been described as button-holed or funnel-shaped on section, and have sloughing bases. Stretches of healthy mucuos membrane intervene between the affected areas. Ulcers often coalesce, and as a result large tracts of the mucosa may present a worm-eaten aspect. In advanced cases thrombosis of vessels occurs, the ulcers may be covered with necrotic sloughs, and the bowel wall at these places considerably thinned. The gut, on the whole, is much thickened throughout the affected area as a result of exudation and œdema. This specially applies to the region of the cæcum which, on palpation, may closely simulate an appendix abscess, tuberculosis, or carcinoma of the colon. These few notes will serve to illustrate points in the pathology and treatment of the disease.

Diagnosis.—Apart from what can be gathered by an inspection of the stools and from clinical symptoms, the diagnosis depends on the detection of *E. histolytica* in the motions. Without going into details, it may be said that dysentery amœbæ in warm and undecomposed stools are actively motile and may contain ingested red cells. These qualities serve, in unstained specimens, to distinguish them from the harmless but common *E. coli*, which is not so motile and never contains red blood corpuscles, and from the macrophage cells commonly seen in bacillary dysentery stools; these may contain red blood cells but are non-motile. Other entamœbæ which resemble *E. histolytica*, but are non-pathogenic, are shown in Fig 33. The stools of amœbic dysentery are rich in motile micro-organisms and eosinophiles (Plate 15).

A culture medium for *E. histolytica* has recently been perfected, and a complement fixation test in which the patient's serum is put up with an alcoholic extract of cultures of *E. histolytica* has also been under trial. But repeated microscopic examination of the stools remains the routine diagnostic method for day-to-day purposes

Differential Diagnosis.—From bacillary dysentery by microscopic examination of the stools and bacteriological tests The mucus of the bacillary dysentery stool practically wholly consists of an exudate made up almost entirely of pus, intestinal epithelial cells, and large macrophages (Plate 16) This is not a feature of the mucus of the amœbic stool Clinically the diseases can rarely be differentiated, though a severe onset and rise of temperature suggest the bacillary form. The idea that a diagnosis can easily be made from the mere appearance of the stools is entirely fallacious, but it is true that the large number of pus cells in the mucoid stool of bacillary dysentery tends to give it a whitish appearance, while in amœbic cases the colour is brown or greyish green As stated, the blood in the amœbic is darker than in bacillary cases It must be remembered that the excretion of *E. histolytica* is frequently intermittent, hence several examinations of the fæces at appropriate intervals are often necessary

In doubtful cases an examination with the sigmoidoscope may clear up the diagnosis.

One form of intestinal amœbiasis, fortunately *not very common*, may closely resemble acute appendicitis.

The onset, which may be acute and accompanied by slight fever and a variable leucocytosis, is marked by colicky pain of varying intensity in the right iliac fossa. The patient may be constipated for several days and the stools, when passed, are often not characteristic. After a few days a distinct lump, usually sausage-shaped, may be felt in the region of McBurney's point. This lump, which is a swollen and œdematous cæcum, may closely resemble an appendicular abscess. But the guarding and rigidity over the lump are usually less marked than over an abscess, and the tumour is often relatively mobile. Although laparotomy may be necessary if the diagnosis is in reasonable doubt, it is most unwise to perform an appendicectomy in the presence of a swollen and œdematous cæcum unless the condition of the appendix urgently demands it. The unhealthy œdematous cæcum characteristic of amœbic "typhlitis" is markedly intolerant of rough handling and many disasters have followed unwarranted operations in this neighbourhood. Sooner or later, if the condition is due to amœbiasis, the characteristic stools containing *E. histolytica* will be passed.

Complications.—Hepatitis, liver abscess, amœboma, hæmorrhoids, intestinal gangrene, peritonitis, and hæmorrhage may be mentioned. The attack may be followed by chronic constipation accompanying a condition known as "dry recto-colitis," in which emetine has been found beneficial.

Primary or metastatic pulmonary amœbic abscess is a doubtful entity although continental writers often report it. Pulmonary abscess in connection with amœbiasis is usually situated near the base of the right lung and is almost invariably due to direct spread by way of the diaphragm from an underlying liver abscess.

Cutaneous Amœbiasis.—A rapidly spreading ulcerative process involving the skin may occur:—

(1) About the anus in cases of amœbic colitis or dysentery.
(2) Subsequent to drainage of an amœbic abscess of the liver.
[illegible] wound.

[illegible] includes also anal pruritus, urticaria, and acne rosacea.

All these forms of cutaneous amœbiasis usually respond satisfactorily to treatment with emetine.

[illegible] a [illegible] all [illegible] The inflammatory process spreads around the bowel, and the resulting mass consists of granulation and fibrous tissue. It often contains many small abscesses. The commonest sites of amœboma are the cæcum, flexures of the colon, and the rectum, especially the region of the recto-sigmoid junction. Being largely a proliferative lesion the amœboma may project into the lumen of the gut as an ulcerating fungating tumour or form an

annular constricting band. In either case, especially if the lesion is in the colon or cæcum, obstructive symptoms may result. There is often no clear account of preceding dysentery and the differential diagnosis from carcinoma may be extremely difficult and often impossible by macroscopic appearances alone, even when the mass is in the rectum or pelvic colon within easy reach of the sigmoidoscope or proctoscope. In all doubtful cases, if the lesion can be brought within view by the sigmoidoscope, a biopsy should be carried out, care being taken to bite off a sizeable portion of the mass containing more than merely the inflamed mucous membrane. For colonic lesions outside the range of the sigmoidoscope, laparotomy may be necessary, with possible excision of the section of gut containing the tumour. In all cases, before the patient is subjected to a mutilating and possibly unnecessary operation, the effect of emetine injections should be tried, since many of these granulomatous masses literally melt away under the influence of this drug. Recently, the use of penicillin in long-standing cases has spared many patients from large operations, tumours which have not responded to emetine at first have disappeared completely when the emetine has been given again after a course of parenteral penicillin.

Hæmorrhoids.—Internal and external hæmorrhoids may be associated with intestinal amœbiasis. In the presence of active amœbiasis it is extremely unwise to attempt operative or injection therapy for these hæmorrhoids. The results are usually unsatisfactory and may be disastrous.

Prognosis.—Untreated or wrongly-treated cases may go from bad to worse, become chronic, or lead to liver abscess. The importance of early, correct, and efficient treatment cannot be overrated. Carefully wash the stools and examine for sloughs from time to time, as their presence or absence shows how the case is progressing.

It must be remembered that amœbic dysentery is very prone to relapse.

Dietetic Treatment.—Milk can be given almost from the first in most cases of amœbic dysentery, and a low-residue but nourishing diet a few days later.

Give food in small quantities frequently, and see that it is neither too hot nor too cold. Alcohol is hurtful.

Medicinal Treatment.—An account of the medicinal treatment of amœbic dysentery falls naturally into two parts—the drugs available, and the treatment-courses recommended for particular types of case.

Drugs Available

Emetine hydrochloride.—Undoubtedly the most effective remedy for controlling the acute symptoms. One grain, dissolved in sterile water, is given hypodermically or intramuscularly every day, either in one dose or divided into two half-grain doses. The total amount of emetine administered in any one course should not exceed 12 grains, gr 1 daily for four to six days is usually enough to control the acute symptoms. The patient should be kept strictly in bed while taking emetine in view of the possible ill-effects on the heart.

Prolonged or repeated courses of emetine must not be prescribed recklessly, for the drug may cause various unpleasant and serious symptoms, which include depression and debility, cardiac disturbance, and even peripheral neuritis with paralysis affecting the legs and arms. Sometimes emetine has curious effects on the nails, causing ridging and great enlargement of the basal lunule.

Among other side-effects of emetine are fine desquamation of the skin, and occasionally diarrhœa. It is important to remember that diarrhœa is occasionally due to emetine and not suppose that it is evidence of need for more energetic treatment of the dysentery for which the emetine was originally given.

A course of emetine injections is followed at once by a 10 to 12 days' course of emetine bismuth iodide (E.B.I.) and yatren.

Emetine bismuth iodide.—This compound contains one grain of emetine in every three grains. The usual course is one dose of three grains daily for 12 consecutive days.

It is important to remember that some commercial preparations of emetine in pill form may be passed unchanged. The stools must be inspected for blackening to confirm that the capsules or pills are disintegrating satisfactorily.

Nausea and vomiting must be expected early in the course. Indeed, their absence should arouse suspicion that the capsules or pills are not

diarrhœa, but this rarely requires any treatment. A patient on E.B.I. treatment may be allowed up to go to the lavatory, otherwise he must remain in bed during the course.

Diodoquin is a tasteless non-toxic compound containing 63.9 per cent. iodine, it has been used with success in the treatment of chronic intestinal amœbiasis. Patients under treatment with this remedy occasionally

use would appear to be in the treatment of patients who have ... received repeated courses of emetine without effect or as a substitute for

* British equivalents—Chiniofon B.P., Quinoxyl, Quiniosulphan.

chiniofon (yatren) if, for any reason, the retention-enema is not well tolerated.

Auremetine, a compound of emetine with the dye, auramine, is recommended by some clinicians. It is given as a powder in capsules by mouth in one grain doses until a total of gr. 40–60 has been reached.

The preparations stovarsol and carbarsone (next to be described) are beneficial as follow-on treatment after emetine, or they may be given with some form of emetine in a combined course. They are especially useful for patients who are suffering from the effects of prolonged treatment with one or other of the ipecacuanha derivatives.

Stovarsol (acetyl-oxy-amino-phenyl-arsenic acid) may be given in 4-grain doses once or twice a day by mouth, either alone or in conjunction with one of the emetine preparations A 12-day course is usually recommended Unlike emetine, stovarsol is an excellent general tonic. Some persons are intolerant of the drug and may develop an erythematous or papular rash, or even a severe dermatitis. Optic atrophy has followed overdosage.

Carbarsone (4-carbamino-phenyl-arsenic acid) is allied to tryparsamide and stovarsol The dosage and indications are the same as for stovarsol The clinical action is due to the content of arsenic and it is said to be less toxic than stovarsol and more effective.

Sulphonamides and penicillin.—There is good evidence that invasion of the damaged intestinal wall by secondary pyogenic organisms plays an important part in the chronic case that is intractable to ordinary combined courses of treatment with emetine, E B I , and chiniofon But Hargreaves has shown that preliminary treatment with sulphonamides and penicillin may bring about conditions that permit a favourable response to emetine therapy in patients who have resisted all ordinary forms of treatment and have progressively deteriorated into a poor state, both physically and mentally. For details *see* course C described under Courses Recommended (below)

COURSES RECOMMENDED

Treatment of amœbic dysentery should begin as soon as possible after the diagnosis has been made and the patient has been got under conditions that allow his treatment to be satisfactorily carried out—that is, as soon as he can be got under proper nursing and kept strictly in bed during the emetine treatment According to the stage of the disease when it comes under treatment, one or other of the three courses A, B, or C, is recommended.

Course A (for acute cases with vegetative E. histolytica in the stools).—Emetine hydrochloride grain one daily by hypodermic injection for four to six days is usually enough to control the acute symptoms. Without any interval, this should be followed by the oral administration of emetine bismuth iodide (E B I) in doses of grains three daily for 12 consecutive days Great care should be taken to ensure that the E.B I. is given in suitable form. Inspection of the stools should be made regularly to see that the pills or capsules are not being passed undissolved, it may be

emphasized that E.B.I. must blacken the stools *if the pills or capsules are* disintegrating properly. Along with the E.B.I. a chiniofon retention-enema preceded by an alkaline washout (2 per cent. sodium carbonate) [illegible]

[illegible] is well tolerated. The *important point is that the enema should be* retained by the patient for at least six hours and to ensure successful retention he should be kept at rest during this period. If diodoquin is available *it should be used if for any reason the chiniofon enema is not* well tolerated, three tablets, each containing grains 3·2 (0 2 gramme) should be given three times a day for 20 days.

[illegible]

convalescence. While emetine injections are being given he must remain strictly in bed; when these injections are finished but the E.B.I. is still be [illegible]

tic [illegible] ticularly acute attack. *In this circumstance it is of benefit to give sulphaguanidine or sulphasuxidine (succinyl sulphathiazole), 5 grammes* 4-hourly, along with the emetine injections.

Course B (for patients who are passing cysts but not vegetative forms of E. histolytica *and who present neither acute dysenteric symptoms nor indications of hepatitis).*—The hypodermic injections of emetine are omitted. Treatment by oral E.B.I. with retention-enemas or diodoquin *and the follow-up course of stovarsol or carbarsone is begun at once* and carried through as in course A.

Course C (for intractable cases that resist ordinary treatment).—Cases of amœbic dysentery that resist course A *will usually respond to it after a pre*-liminary course of penicillin and sulphasuxidine has eliminated secondary [illegible] diseased bowel [illegible] ts of penicillin [illegible] it with 33,000 [illegible] n given. The [illegible] ry four hours [illegible] azine, sulpha- [illegible] te dosage as [illegible] a new com- [illegible] ch resist these [illegible] ow a suitable interval and then repeat the whole course.

Criteria of cure.—Amœbic dysentery is notoriously liable to relapse. *Stools should be examined macroscopically at regular intervals during* treatment and microscopically on six consecutive days at least two weeks after all treatment has been completed, this interval between the end of treatment and the beginning of the laboratory clearance tests is important.

Sigmoidoscopic examination for test of cure should likewise be defer until the same time

General considerations —Correctly given drug-therapy should be sup ported by a cheerful ward-atmosphere and good nourishing food Mil may be given from the first and followed as soon as possible by a nutritiou low-residue diet of high caloric value. Vitamins in some form—multivite tablets, for example—may sometimes have to be added

Prophylaxis —The general measures of prevention are much the same as those required for bacillary dysentery (*see below*) It should be emembered that it is the cyst-carrying convalescent and the healthy arrier who constitute the real danger rather than the actual patient under eatment in hospital Ideally, none with a history of having suffered om amœbiasis should be employed in the handling of food or drink It is uncertain to what extent the cysts of *E histolytica* are conveyed by ter but outbreaks of amœbiasis apparently due to defective water plies have occasionally been reported

The standard methods of sterilization of water by chlorination do not kill cysts, filtration or boiling is necessary to ensure their removal or destruction

Yorke found the following solutions lethal for cysts both at 37 C and at ordinary temperatures —$HgCl_2$, 1 in 2,500, formaldehyde 0 5 per cent , carbolic acid and lysol, 1 per cent Cysts kept in fæces at ordinary temperatures die within ten days and in water in three weeks

Hepatic Amœbiasis

The records of fatal cases furnish grim evidence that amœbic abscess of the liver too often goes unrecognized until it is too late to avert death Every death from this dangerous form of amœbiasis represents a failure to diagnose and treat the condition in its early phase when it responds so readily to suitable measures

Abscess formation is the end-result of a progressive lesion that has almost certainly begun with intestinal ulceration although this need not have given rise to clinical dysentery The initial change in the liver is one of non-suppurative hepatitis, which generally responds quickly and well to injections of emetine In the final stage of pus formation, this response is unfortunately much less certain

Clinical dysentery (intestinal amœbiasis) may precede the onset of hepatic symptoms by days weeks, months, or even years uncommonly it appears at the same time Quite often there is no more than a history of some earlier diarrhœa, less often there is no story whatever of any previous intestinal disorder

Symptoms and localizing signs. —The onset of hepatic amœbiasis is often insidious and the symptoms and signs are notoriously varied and equivocal A successful diagnosis is often the outcome of nothing more definite than constant awareness of the condition and a full realization that it is not excluded because a previous history of intestinal symptoms is lacking or even because there are no localizing signs in the liver.

Considerable diagnostic significance attaches to any abnormal signs

that may be discovered at the base of the right lung such as congestion, consolidation, or pleurisy with or without effusion. These signs are often found along with amœbic hepatitis and unless this is recognized their discovery may distort or even hide the true diagnostic picture. In recent times, sulphonamides have sometimes been given instead of emetine to patients with such signs; the results have naturally been disastrous and tragically avoidable.

Fortunately, hepatic amœbiasis is not usually silent and its presence is revealed by a number of localizing symptoms and signs. The more important of these are given below.

(1) *Pain* may be present with or without tenderness; it can be general or localized over some part of the liver area; often it is most marked along the lower border of the enlarged liver. This pain may be noticed only at night and it is often produced or aggravated by sudden movements such as turning in bed. In some early cases, a localized area of tenderness no larger than a shilling may be discovered by careful palpation over the liver area, often on its anterior surface. This small tender zone, which the patient may not have perceived until it was discovered by careful palpation, is of considerable diagnostic importance, its exact location should be noted for reference because it may be the site of a future abscess. If shoulder pain is present, it is usually felt on the right side, often only at night.

(2) *Hepatic enlargement.*—The liver may increase in size and the enlargement may be upwards, downwards, or in both directions.

(3) *Signs of lung abscess.*—If a liver abscess situated immediately below the diaphragm bursts into the lung, the signs and symptoms of lung abscess will be added to those already described. In the early stages, spitting of blood may raise suspicions of pulmonary tuber- [illegible] especially if recognition of the true nature of events leads to administration of emetine by injection.

Constitutional Symptoms.—Generalized symptoms of toxæmia are the [illegible] fever. The pyrexia is often slight at first, later it [illegible] assumes a swinging character. Drenching sweats, often preceded by rigors, may closely simulate acute tuberculosis or malaria. Indeed few long-standing cases of amœbic abscess have escaped being soaked with quinine and this may produce temporary improvement if malaria is also present. Malaria and some stages of amœbic abscess are very alike in their symptomatology but too many of the alleged cases of quinine-resistant malaria are in reality double infections with *Plasmodium* and

Entamœba. It is essential to be alive to this diagnostic pitfall in order that the correct treatment may be given and life saved.

Exceptionally, *in debilitated, non-reacting persons who have lived many years in the tropics*, a liver abscess may run its course and *end fatally without either pyrexia or localizing signs in the liver*; and this may cause great difficulty in diagnosis. These people have a muddy complexion, a *toxic appearance*, a dirty tongue, constipation, progressive loss of weight, and faulty concentration. They become more and more easily tired and finally unable to carry on their daily routine duties. They are invalided home with the faulty diagnosis of "tropical neurasthenia", *only to die soon after from an undisclosed liver abscess*.

Jaundice is not common at any stage of an uncomplicated liver abscess, the toxic, muddy appearance of the complexion is the characteristic feature.

Diagnosis.—The following investigations are important aids to diagnosis and they should be carried out in doubtful cases, a negative finding in any or all of them is not sufficient reason for discarding amœbic abscess as a possibility.

(1) *Total and differential white blood count* usually shows a moderate leucocytosis of 12,000–20,000 per c.mm. Polymorphs are usually in normal proportions (65–75 per cent); any marked increase of polymorphs (80 per cent or more) suggests the onset of secondary pyogenic infection.

(2) *Sigmoidoscopic examination* may reveal scars or ulcers as evidence of past or present amœbic ulceration of the large intestine. If an ulcer is seen it should be swabbed in order to determine if amœbæ are present. It must be remembered that less than a quarter of the total length of the large intestine is within reach of the sigmoidoscope, unfortunately the non-visible portions include the cæcum, which is by far the most important site of intestinal amœbiasis

(3) *Stool examinations* should never be omitted, for the presence of [illegible]

may reveal vegetative forms but more often cysts of *Entamœba histolytica*. Vegetative forms are rarely found if the stool is solid, they are more often discovered in a liquid stool passed in response to a dose of salts.

(4) *Radiological examination*.—Screening should be carried out and films taken. One or more of the following may be found: diminished movement, paradoxical movement, or raising of the right cupola of the diaphragm, abnormal contour ("humping") of the raised right cupola, abnormal signs at the base of the right lung that indicate effusion, congestion, consolidation, [illegible]

or lung abscess; and increased acuity of the right costo-phrenic angle.

(5) *Therapeutic test.*—If there is reasonable suspicion of hepatic amœbiasis, a course *of emetine injections is justified even in the* complete absence of positive signs. This procedure, sensibly and judiciously applied, will avert many tragic deaths.

Left Lobe Abscess.—The majority of single liver abscesses are situated in the upper and posterior aspect of the right lobe in fairly close relationship to the right cupola of the diaphragm. Most of the symptoms already described are determined by this location and relationship. The rarer *abscess of the left lobe tends to develop near the under surface of the left* lobe and it may present as a palpable mass beneath the left costal margin or in the epigastrium. Often, this mass will give the impression of having no direct connection with the liver; by pressing on the stomach, it may produce symptoms and radiological appearances highly suggestive of gastric neoplasm. These include anorexia, vomiting, wasting, achlorhydria, epigastric pain, and tenderness. An X-ray following a barium meal usually shows a gastric filling-defect of the "soup-plate" variety. This appearance should suggest an extrinsic tumour pressing on the stomach, but it is often mistakenly accepted as proof of a tumour within the stomach.

Occasionally, *by distorting the stomach and binding it by adhesions*, a liver abscess may produce a filling-defect extremely suggestive of intrinsic gastric neoplasm even to those who are fully alive to the different appearances associated with tumours inside and outside the stomach.

Differential Diagnosis.—It is impossible here to mention all the conditions from which liver abscess has to be distinguished. It is particularly important to remember malaria and malarial hepatitis, basal pleurisy, *inflammatory* and suppurative states of the gall bladder, hydatid cysts, appendicitis, syphilis or neoplasm of the liver, tuberculosis (especially perhaps Addison's disease), scurvy, kala-azar, and undulant fever. Liver abscess may complicate enteric infections, especially those due to *Bact. paratyphosum C*

Treatment.—Only the vegetative stages of *Entamœba histolytica* are ever found in the liver; cysts have never been discovered in a liver abscess. This is fortunate for treatment because the vegetative stage is far more [illegible] than the cysts. Largely for this reason, [illegible] nation, are [illegible] t must not [illegible] may need longer and repeated courses of [illegible] the pre- [illegible] form emetine [illegible] to [illegible]

is, the 8th to 10th interspace in the mid-axillary line. Pre-medication with morphine and hyoscine or some other sedative is usually advisable; local anæsthesia is employed for the needling. If pus is found on exploration, an effort is made to drain the abscess cavity with a Potain's or other closed aspirator. Several such aspirations may be necessary at intervals of a week or more. In exceptional cases repeated aspirations fail to effect a cure and the patient continues to go downhill, use must then be made of some form of closed suction drainage, or, as some surgeons prefer, open drainage with removal of one or more rib sections.

It must be remembered that there may be more than one abscess to drain. It is worth noting that after pus has been evacuated from a large abscess shrinkage of adjacent liver tissue may greatly raise the cavity. Later aspirations must then be done at a higher level, or, with open drainage, a new and higher incision may become necessary.

If repeated aspirations fail to locate a reasonably certain right-lobe abscess, or if a left-lobe abscess is diagnosed, exploratory laparotomy should be considered before the patient's condition deteriorates too far.

Air Replacement.—Valuable information has sometimes been gained about the size, extent, and communications of a liver abscess by replacing the pus with air or lipiodol and following this by radiological examination with the patient in various positions. But this technique, although valuable for diagnosis and prognosis, is not without risk and it should not, therefore, be undertaken as a routine measure, it is appropriate only if some special information is required and if this cannot be elicited by any other means.

BACILLARY DYSENTERY

The cause is usually either Shiga's bacillus or bacilli of the Flexner or Sonne type. Others may be operative, but do not require mention here. Shiga infections are the most serious because of the potent exotoxin formed. Rarely *B. dysenteriæ* may be found in the peripheral blood.

Like typhoid, the spread of bacillary dysentery may be said to be due to "careless carriers, contact cases, chiefly cooks, dirty drinking water, the dust of dried dejecta and the repulsive regurgitation, dangerous droppings, and filthy feet of fæcal-feeding flies fouling food." In this connexion it may be noted that dysentery bacilli have been recovered from flies two or three days after their ingestion by these insects.

Symptoms.—The incubation period would appear to vary from twenty-four hours to seven days. The symptoms vary greatly according to the severity of the attack. In the very mild cases the illness may be confined to the passage of loose motions, containing little or no blood or slime, associated with only slight fever or none. In the more severe cases, however, the onset, which may follow a premonitory diarrhœa or constipation, is sudden and attended by pain and an urgent call to stool. At first the motions are normal, but as the attack advances the colic grows more severe, straining and tenesmus set in, there is diarrhœa, and soon the fæculent matter is mixed with bright red blood and mucus, while

the blood and mucus predominate and finally constitute the whole motion. *There is great discomfort about the anus,* which becomes inflamed, excoriated, and very painful, and the bowel may prolapse. Vesical tenesmus may occur and the urine is diminished in quantity. The tongue is moist and coated with a white fur, nausea is frequent, *vomiting comparatively rare.* The temperature usually rises and may be considerably elevated, a contrast to what occurs in the amœbic form. The number of stools is generally from fifteen to thirty in the twenty-four hours, but it may become excessive and exceedingly exhausting to the patient. The thickened bowel may be capable of palpation if the abdomen is not too tender. As already stated, the stools, being markedly muco-purulent, are often white like milk, but they *are rarely free from blood, which usually* occurs as flecks or streaks.

When the small intestine becomes involved, for this sometimes occurs and is very dangerous, the temperature remains elevated and general symptoms are much more severe, though the tenesmus is less and the stools fewer. In ordinary ulcerative cases the prognosis depends on the quality rather than on the quantity of the stool. The patient is often heavy and drowsy and exhibits rather a characteristic bluish-red flush on the cheeks. Such cases are usually Shiga infections. It is well to remember that the small intestine, if not involved, may be full of fæcal matter, *i.e.* there may be a local spasm accompanying the diarrhœa and causing distension.

[illegible] and offensive sloughs be passed. Toxæmia is then usually very marked, the tongue becoming dry and glazed, the pulse thready and a low muttering *delirium supervening. Hiccup may set in and prove exhausting.*

It will be seen that bacillary dysentery tends to be more acute and more toxæmic than the amœbic type. Cases may be classified on a clinical basis, as · 1 Mild (patient apparently well but passing a little blood and mucus). 2. Catarrhal. 3. Ordinary ulcerative. 4 Fulminating. 5. Choleraic (Fisher). In toxæmic cases the diarrhœa is of secondary importance to the toxæmia.

[illegible] neurasthenia.

Morbid Anatomy.—In the earlier stages the appearance of the mucous membrane of the large intestine has been aptly compared to lustreless red velvet. *This is due to an acute inflammation* which may also involve the *lower third of the ileum, although Peyer's patches remain unaffected.* Later there are areas of blood extravasation beneath the surface and irregular islands of greyish membrane surrounded by hyperæmic and swollen gut. The condition is one of diffuse superficial *coagulation* necrosis, and the small ulcers are not deep as in the amœbic form. When necrosis is advanced nothing is left of the mucous membrane but a dark

green or blackish substance which contains no vestige of gland tissue. This stage of absence of secreting glands is shown clinically by the absence of mucus in the rectal discharges which now have the appearance of "meat washings".

The other viscera exhibit signs of the acute toxæmia which is such a feature of the condition.

Diagnosis.—Macroscopically the stools contain or consist solely of blood and tenacious mucus. In extreme cases there are simply red streaks or specks in a whitish medium which adheres to the bottom of the receptacle. The blood is bright red, the stool odourless—an important point. Later the mucus assumes a yellow tinge and bile or liquid grey fæces may be present. In bad cases offensive green necrotic sloughs may appear and at this stage the stool may resemble that of amœbic dysentery.

Microscopically many undamaged pus cells and red cells are seen, together with large refractile macrophage cells derived from the sub-mucosa and often containing red blood corpuscles and polymorphs. These cells have again and again been mistaken for dysentery amœbæ. There is often an absence of motile micro-organisms (Plate 16).

The bacteriological diagnosis cannot be considered here.

Sigmoidoscopy should never be forgotten if the diagnosis remains in doubt.

Differential Diagnosis.—That from amœbic dys[illegible] tioned. Schistosome dysent[illegible] chronic cases [illegible] excluded from [illegible]

Malarial dy[illegible] due to subtertian infection, has rather characteristic symptoms, well described by Manson-Bahr as follows —

"The onset is sudden, and is accompanied by pyrexia and a rigor, and it may be by vomiting. During the course of this the patient is seized with violent central abdominal pains, and passes stools composed of blood clots and bright blood-stained mucus The stools may not exceed six in the twenty-four hours. They are composed of red blood corpuscles in rouleaux and columnar epithelial cells, pus cells are absent. This fact alone should make one suspicious that the case is not one of bacillary dysentery.

"Of course a blood slide will reveal the presence of the subtertian parasite, both in the ring and crescent stage. The spleen may, or may not, be enlarged according to the length of time the malarial infection has existed. There is something in the look of the patient that should make one suspicious, the sweating and icteric tint of the sclerotics and skin.

"It is essential that one should be on the look-out for these cases, for unless promptly diagnosed and treated with quinine they may prove rapidly fatal."

It is important to remember the possibility of malarial dysentery as these cases may find their way into a dysentery ward where malaria is not suspected and routine blood smears are not taken.

Complications.—Intestinal gangrene, peritonitis, eye affections, arthritis, rheumatic symptoms, and polyneuritis may be mentioned The last

named, which may be associated with œdema, tends to pass off as the ulcerations heal up. An acute suprarenal syndrome has been described.

In true dysenteric arthritis it is usually the larger joints such as the knees, elbows, etc, which are attacked. This complication, which is

especially attacked, although almost every joint in the body may be affected. Serum arthritis is transient and rarely lasts more than two or three days. One of the commonest complications

times up to six weeks after its termination. The attack of dysentery—usually Shiga or Flexner—need not necessarily have been severe; the

function was the rule.

Prognosis.—The prognosis of bacillary dysentery, especially of the severe Shiga infections, has been revolutionized by the advent of the sulphonamides. Nowadays one rarely sees a moribund case of this disease if sulphonamides have been available. If treatment with an appropriate sulphonamide is begun early and persevered with the prognosis is almost invariably good. The small minority who fail to respond to sulphonamide therapy are usually found to be suffering from some infection other than bacillary dysentery—ulcerative colitis or intestinal amœbiasis, for example.

Prophylaxis.—*General.*—Infection with dysentery bacilli is usually due to ingestion of infected food, though water and drinks of various kinds may also be responsible.

Fly-contamination of food, drink, and feeding-utensils must be avoided. Fly-prevention, therefore, is of the highest importance and all the measures detailed in the section dealing with this insect should be carried out. The most careful attention should be paid to the fly-proofing of latrines; the proper disinfection of the excreta of patients in hospital and elsewhere is of great importance. (*See* Arthopod pests and Appendix I.)

Contamination of food and drink by healthy carriers or mild cases should be guarded against by measures indicated below. Contamination by dust and dirt must similarly be prevented.

lost sight of.

In the tropics and semi-tropics, vegetables, especially lettuces, are a serious risk and should never be eaten uncooked. Fruits which are

skinned before being eaten are not normally dangerous, but other types are, and care must be taken to ensure that they are sterilized before being eaten by steeping them in strong bleach solution followed by thorough washing. The same precautions must be taken with vegetables that are liable to contamination with human excreta.

The fullest attention must be paid to cookhouse sanitation and cleanliness of cooks

The dangers of civilian cafes, restaurants, and the like cannot be overemphasized, for much dysentery is spread by these establishments Their fullest possible control is, therefore, of paramount importance Hawkers of food and drink are even more dangerous.

Ice is not often a cause of the spread of dysentery but it may be infected and should not be put into drinks unless it is known to have been prepared from a safe water supply.

Finally the purity of the water supply must be ensured.

Special—Early treatment of all diarrhœa with sulphaguanidine with a [illegible]

Alternative schemes are given under Sulphonamide Drugs (p. 319 and on p 116). Those who have not recovered at the end of this period should be admitted to hospital.

A similar procedure may be followed with mild cases of dysentery, especially in epidemics when difficulties in hospitalization may arise.

[illegible]

handling of food and drink, to ensure this, it is necessary to carry out medical examinations of all cookhouse and dining-hall personnel, whether [illegible]

Treatment.—*Medicinal and General.*—For any severe case, absolut [illegible]

has now been almost entirely superseded by sulphonamide therapy

Sulphaguanidine has been chiefly used in this country while other members of the group such as succinyl sulphathiazole (sulphasuxidine) and sulphadiazine have found favour in America. The usual dosage of sulphaguanidine for severe cases is an initial dose of 7 grammes (i.e. 0.1 g. per kilo of body weight for a man of average weight); then 3.5 grammes every four hours day and night until the stools are reduced to five or less daily; the same maintenance doses can then be given at 8-hourly intervals for at least a further 72 hours.

For mild cases an initial dose of 4–6 grammes with a maintenance dosage of 2–3 grammes often suffices.

In the past "heroic" total doses of sulphaguanidine (up to 600 grammes or more) have been given. But experience has taught that a total dosage of more than 100 grammes, extending over a week or ten days, is rarely justified. If the patient fails to respond to this dosage it is usually

dysentery bacilli in the lumen of the large gut because it was poorly absorbed, but it is now known that appreciable absorption takes place—although slowly—and that toxic symptoms may result from such absorption. Among these may be mentioned: *obstruction of renal tubules by crystals, causing urinary suppression*; various rashes; and, in at least one case, acute transient psychosis due to over-dosage.

During treatment with all sulphonamides, including sulphaguanidine, *it is of prime importance to ensure a liberal fluid intake, especially under hot-weather conditions.* If for any reason sufficient fluid cannot be introduced by mouth, the parenteral route must be used. This will greatly diminish if not abolish incidence of renal blockage leading to urinary suppression, a special danger in hot countries.

The danger of toxic side-effects can be *reduced if facilities exist for periodic estimations of the blood sulphonamide.*

eight hours of
nal pain and
tenderness, and the consequent lessening or disappearance of abdominal symptoms.

2. A reduction in the temperature and pulse rate, which often reach normal in one to three days.

... in the number of stools: often within five

reduction in the mucus present.

The earlier this treatment is commenced the more rapid ... recovery. Neverthele... not beer ... the resul...

It is ... proviso ... bring abou...

If sulphaguanidine is not available ...

...

...iophage by the oral route has been tried in a number of different localities, but has proved disappointing

If pain and want of sleep threaten to exhaust the patient's strength, do not hesitate to give morphine

Simple lavage of the lower bowel is very comfor... the case, the bowel ... cocain ... easier

It is ... bacillary dysentery, more especially ... become serous ... be very ... pints, to ... added ...

Some ... advocate 25 per cent. solutions of glucose in distilled water given intravenously They are said to act better than saline

Serum.—In Shiga infe... is given ... delay ... the intestinal mucous membra... completely necrosed, no benefit will follow its use. It is doubtful if it does any good after the third or fourth ... injection of concentrated ... 100,000 units fo... most important ... be obtained ... enzym... reacti...

The ... sulphonamides against dysentery bacilli has greatly diminished the necessity for dysenteric antitoxin but dual therapy with antitoxin and a sulphonamide should always be used in severe Shiga dysentery

The *diet* restrictions formerly imposed on cases of acute bacillary dysentery are now seldom required beyond the first 24 to 48 hours. While

he is on sulphonamide therapy it is important to ensure that the patient takes a liberal supply of fluid.

It is of great importance to ensure that the patient with sub-acute or chronic dysentery is not kept too long on a semi-starvation diet or he will inevitably develop evidence of malnutrition such as sprue, hypoproteinæmia, vitamin-B-complex deficiency, or such like. A well-balanced nutritious diet of high vitamin content and a sufficiency of first-class animal protein should be given as early as possible.

Treat *chronic cases* by lavage of the large bowel. Eusol is suitable, starting with one or two pints in a dilution of 1 ounce to the pint of water, and increasing the quantity and strength daily. Carefully graduate the diet, making systematic naked-eye and microscopical examinations of the stools so as to gauge the patient's power of digestion and absorption. Few people chew their food sufficiently, and in chronic dysentery the symptoms may be kept going and aggravated by careless mastication. Patient and unwavering insistence on this point may result in an almost incredible improvement in the patient's condition.

In chronic cases which have become marasmic, the administration of glucose solutions (5 to 10 per cent.) will often be found beneficial. They [illegible]

Flagellate Diarrhœa

The more important flagellates of the human intestine are shown in Fig 33 The only one of these which is generally regarded as pathogenic is *Giardia intestinalis*. Its habitat is the upper part of the small intestine, and at times it appears to be the cause of a persistent and *troublesome diarrhœa*. On the other hand, *Giardia* may be present in enormous numbers without causing any symptoms whatever. Do *not* forget, as [illegible] that *Giardia* may hide the presence of the [illegible] ...mas, [illegible] ...wel, [illegible] ...tem- [illegible] will eradicate a *Giardia* infection in many cases, while the symptoms may be relieved by bismuth salicylate, 20 grains thrice daily, or by Stovarsol, 8 grains daily.

Ciliate Dysentery

This is due to *Balantidium coli* (Fig. 33, Nos. 30, 31), but is so rare that it requires no further consideration here.

No specific treatment has yet been discovered for balantidiasis.

Coccidial Infection

Although there is no definite evidence that the coccidia found in the human intestine are pathogenic, it is conceivable that as they are *parasites*

[To face p. 118]

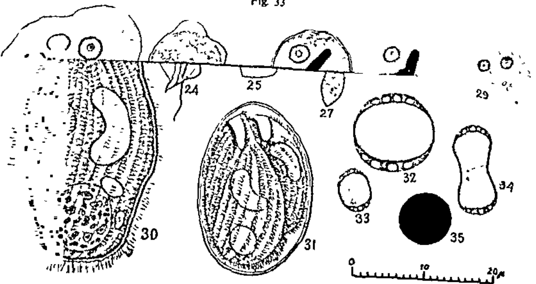


Fig. 33

of intestinal epithelium they might become so under certain conditions. Hence, an illustration of the extracorporeal development of *Isospora* is given in Plate 17.

fat and a large number of Charcot-Leyden crystals is said to be characteristic of infestation with this parasite.

DESCRIPTION OF FIG. 33. (Protozoa of Human Gut.)

(Diagram compiled from various sources.)

All the organisms have been drawn to one scale (shown at bottom of Figure), with the exception of Nos. 30 and 31, which are only half the size of the others. An ordinary human red blood corpuscle on same scale is shown in No. 35 for comparison

Nos. 1–5. *Entamœba histolytica*

No. 1. Large tissue-invading form, containing five red corpuscles

No 2 Small precystic form

No. 3. Cyst with one nucleus and deeply staining chromatoid body

No. 4. Binucleate cyst. (Later stage in development.)

No. 5 Mature cyst, with four nuclei.

Nos 2A–5A represent stages corresponding respectively to Nos 2–5, but belonging to a strain of *E. histolytica* producing cysts of small size Such strains are far from uncommon, but the small cysts are frequently overlooked or mistaken for those of *E. nana*.

Nos. 6–9. *Entamœba coli*

No 6. Large active form, from contents of large intestine. The protoplasm usually contains numerous ingested food-bodies (bacteria, yeasts, etc., from the fæces), but never red blood corpuscles.

No 7 Smaller precystic form, free from food inclusions.

No 8 Cyst containing two nuclei The large clear space is filled, in the living cyst, with a mass of glycogen which stains dark brown with iodine solution.

No 9 Mature cyst, containing eight nuclei.

Nos. 10–13. *Endolimax nana*

No 10. Free amœba, with numerous ingested bacteria in its cytoplasmic vacuoles (Compare the nucleus with those of *E. histolytica* and *E. coli*, Nos 1 and 6.)

No 11 Uninucleate cyst.

No 12. Binucleate cyst

No 13 Mature cyst, with four nuclei. (Compare with No. 5A.)

No. 14 Cyst of *Iodamoeba butschlii*. These cysts are sometimes found [illegible] to be mistaken for those of *E. histolytica*. [illegible] during life with a [illegible] The single [illegible] cytoplasm [illegible] bodies. (*Cf* [illegible] by Wenyon. contains [illegible] No. 3.) These cysts were origin[illegible]

No. 15 Small free-living amœba from old human fæces. Amœbæ of this type occur commonly in decomposing organic matter of all kinds, but are never present in *freshly-passed* human fæces. There are many different species, all of which are commonly, though incorrectly, called "*Amœbalimax*." Note the structure of the nucleus, with its large central karyosome. The clear space in the cytoplasm is a contractile vacuole—never present in any of the amœbæ parasitic in man

No. 16. Cyst of the preceding, with single nucleus, numerous rounded chromatoid masses in cytoplasm, and thick corrugated wall.

Nos. 17–21. **Giardia intestinalis* (=*G. lamblia*)

No. 17. The free flagellate from the contents of the small intestine. Ventral view, showing the "sucking disc" (for temporary attachment the two nuclei, eight flagella, etc.

No. 18. Outline of similar form, seen from left side.

No. 19 Cysts from fæces, containing a single individual.

No. 20 An older cyst, containing two individuals formed by division.

No. 21. A cyst with four nuclei (intermediate between Nos. 19 and 20) as it appears in end view. Such cysts may be mistaken for those of *E. histolytica*. (*Cf*. No. 5A)

Nos. 22, 23. *Chilomastix mesnili*

No. 22. Free flagellate, from large intestine. Note the three anterior flagella, complicated buccal apparatus, etc.

No. 23. Cyst, of typical lemon shape, with single nucleus and remains of buccal structures still present.

Nos. 24, 25. *Trichomonas hominis*

No. 24. Free flagellate, from large bowel, showing undulating membrane, axostyle, etc. Forms with three and five flagella also occur.

No. 25. Degenerate form. The flagellate has lost most of its characteristic structures, and is throwing out a finger-like process, which passes down the body into the dotted positions, and then disappears. This peculiar "undulating" movement may go on repeatedly for hours, or even days, without any change of position occurring.

No. 26. *Dientamœba fragilis*.—A small binucleate amœba which occurs occasionally in man. (*Cf*. No. 2A, 10, 15.)

* *Giardia* Kunstler 1882=*Lamblia* Blanchard, 1888

No. 27. *Embadomonas intestinalis.*—A very small flagellate rarely found in human fæces. It produces a cyst somewhat like that of *Chilomastix mesnili*, but considerably smaller.

Nos. 28 and 29. *Enteromonas* hominis.* The flagellate has three free flagella and one attached trailing flagellum which, however, is sometimes not apparent. It produces a small oval quadrinucleate cyst.

Nos 30, 31. *Balantidium coli*

No. 30. Free ciliate, as it lives in lumen of gut and in tissues.

No. 31. Encysted form passed in fæces. The cyst figured contained two ciliates, but most cysts contain only one.

Nos. 32–34. *Blastocystis hominis*

No 32. Large spherical form.

No. 33. Small oval form.

No. 34. Elongated dividing form.

This organism is extremely common in human fæces. It is of vegetable nature and not a protozoon, and is shown here because it is not uncommonly mistaken for a cyst, or other stage, of one of the intestinal protozoa.

FILARIASIS

The term filariasis is used here as a convenient label for infection with nematodes of the Order Filarioidea. The genus *Filaria*, regarded in the strict zoological sense, comprises only one species, *Filaria martis*, and is not known to affect man. The species *Wuchereria bancrofti*, originally placed in *Filaria*, has been removed from that genus as its characters do not conform with those of the genotype, *Filaria martis*.

Except for *Dracunculus medinensis* (the guinea-worm), the Filarioidea are of little importance as a cause of military inefficiency. Dracontiasis, as guinea-worm disease is called, is found in many parts of Africa, India, Persia, and Brazil, it was troublesome in certain areas during both wars, notably in East Africa, and is dealt with later.

Wuchereria bancrofti is pathogenic in a certain proportion of infections and may give rise to a variety of clinical conditions such as "filaria" fever, lymphangitis, lymphatic varix, enlarged lymph glands, elephantiasis, chyluria, lymphuria, orchitis, chylocele, funiculitis, abscesses, arthritis, synovitis, chylous ascites, and chylous diarrhœa. The possibility of confusing lymphatic varices with herniæ, plague buboes, or syphilitic infection should be borne in mind. Complement fixation and cutaneous tests, with the heart worm of the dog (*Dirofilaria immitis*) as antigen, have given useful results in the hands of Fairley and others.

Secondary pyogenic infection must be stressed as an important factor

* Wenyon points out, from an examination of the original preparations, that as Dobell conjectured, *Tricercomonas* is a synonym of *Enteromonas*

in the production of most of the common obstructive and toxic phenomena of filariasis. Although there is no specific drug for the destruction of filaria, sulphonamides and penicillin have been used with success in the treatment of some of the infective complications. Success has also been claimed with fouadin and other drugs of the antimony series

Many of the later and more chronic complications—elephantiasis, for example—require skilled surgical intervention, although construction by the use of bandaging and elastic stockings may be useful in the early stages.

Prophylaxis —This should consist of the elimination of *Culex fatigans* and its larvæ and the protection of carriers from mosquitoes by nets and other means especially at night. All with microfilariæ in their blood should be looked on as carriers. The vectors of the parasite are given on page 36.

Wuchereria malayi.—Some uncertainty exists whether this is a distinct variety or a variant of *W. bancrofti*.

W. malayi occurs over widespread areas of Malaya, the East Indies, Indo-China, South China, Southern India, Ceylon, etc. It is associated with elephantiasis, especially of the lower limbs.

Vectors are mosquitoes of the genus *Mansonioides* as well as som Anophelines: *An. barbirostris*, *An. hycranus* (var. *sinensis*).

Loa loa is carried by several of the Tabanidæ, *Chrysops dimidiata*, *longicornis*, and *C. silacea*, in which the larva develops in the thoracic muscles. The parasite is widespread in West and Central Africa and heavy infestation of the native population of the Sudan has been noted recently.

Loa loa differs from *W. bancrofti* in that the adult worms infest the connective tissue instead of the lymphatic system and give rise to fugitive subcutaneous swellings about the size of a hen's egg, known as calabar swellings, which last for a few days and then disappear, to recur later elsewhere. Occasionally a worm migrates to the eye, causing local irritation and swelling.

Treatment consists in careful extraction of the worm if it is superficially placed in the eye or elsewhere. The irritation of calabar swellings may be allayed by soothing lotions or by the injection into them of two minims of one in a thousand solution of adrenaline hydrochloride. A high eosinophilia is characteristic of *Loa loa* infestations

Onchocerca volvulus (Africa) and *O. cæcutiens* (tropical America) give rise to subcutaneous fibrous tumours in various parts of the body. The swellings are localized and are easily dealt with by surgical measures. Infestation with *O. cæcutiens*, generally considered to be a Central-American variant of *O. volvulus*, may lead to visual disturbances and even blindness.

The sheathless microfilariæ may be seen with the adult worms, male and female, in the circumscribed subcutaneous tumours or tissues of the eye.

In addition to the above, prurigenous (papular and itchy) and sclero dermatous (ridged and thickened) skin lesions are often met with i

chronic sufferers from onchocerciasis. Section of the affected skin area sometimes shows large numbers of microfilariæ but their presence is inconstant and their causal relationship to the skin lesions uncertain.

Elephantiasis and hydrocele have often been noted, especially in Africa, in association with onchocerciasis but the presence of other filarial infestations could not with certainty be ruled out.

Ocular symptoms are said to appear relatively late in the disease—some years after infection or the appearance of subcutaneous nodules.

Photophobia, epiphora (overflow of tears), and pericorneal conjunctivitis are early manifestations Punctate keratitis and iritis ar occasional early symptoms. Corneal vascularization leading to p (abnormal membrane over the cornea) and complete blindness may in advanced cases.

Actively motile microfilariæ may be seen in the tissues and char of the eye.

Much of the prevalent blindness in the Sudan is said to be due onchocerciasis. Eye lesions are said to be specially liable to develop those who have had subcutaneous tumours on the upper half of the boc being much less common in those whose legs were chiefly affected.

The diagnosis of subcutaneous nodules has to be made from those du to other causes cysticercosis, non-parasitic fibromata, lipomata, juxta articular rheumatic nodules, and so forth. The fluid aspirated from a node may show large numbers of microfilariæ, and sections of the skin, especially in the region of the tumours, may also show them. The histological picture of an excised nodule is typical

Eosinophilia is common in all forms of filariasis

Treatment consists in removal of the subcutaneous nodules whenever possible. It is above all necessary to deal with those in the head and eck region since they are thought most likely to lead to serious eye symptoms Various filaricidal drugs, of which tartar emetic appears to be the most promising, have been tried. The known carriers are given on page 41

Dipetalonema perstans (*Acanthocheilonema perstans*), at one time thought to be non-pathogenic to man, is now considered capable of producing symptoms of the same order as *W. bancrofti* Fülleborn considers that it may also produce calabar swellings. It is a very common parasite in tropical Africa, and in some parts—the Congo basin and Cameroons—up to 92 per cent of the native population may show microfilariæ in their blood It is also found in South America The adults inhabit the mesentery. For the known carriers, see page 41

The embryos (microfilariæ) of *W. bancrofti*, *L. loa*, and *D perstans* are found in the peripheral blood. Except in the Southern Pacific where the vector is a day feeder, the microfilaria of *W bancrofti* observes a nocturnal periodicity, that of *L. loa* is diurnal in habit, while *D perstans* embryos are present in the blood both by day and night, although the numbers found vary irregularly from time to time. The microfilariæ of *D perstans* are much smaller than those of *W. bancrofti* and *Loa loa* and differ from them in being entirely without a sheath In examining blood for microfilariæ always employ some thick-drop method If this fails to demon-

affected limb are usually the only symptoms. Sometimes there are premonitory signs, of which a general or localized urticaria is the most characteristic. A kind of gastric crisis—with gastro-intestinal disturbance, giddiness, and even fainting attacks—has been noted at this stage. Sometimes there is pain and fever, but chiefly as a result of an accident during treatment (*see* Treatment). There is usually a moderate eosinophilia.

In some districts (Bombay) the parasite shows a special *predilection* for the neighbourhood of the large joints, notably the knee and ankle. A septic arthritis occasionally results from secondary pyogenic infection.

Multiple infestations were common and extremely crippling among certain African and Indian formations who fought in the 1939–45 war, prolonged hospitalization was usually necessary.

Prophylaxis.—Infected persons should not be allowed in the close proximity of water supplies, wells should be covered and water holes protected. In endemic areas all drinking water should be boiled. Failing this, filtration through cotton cloth will remove infected cyclops, but it must be properly carried out under supervision. Where it can be done the temperature of the water in wells and water holes can be raised by passing steam into them. A temperature of 65° C. is fatal to the cyclops. The addition of a trace of potash to the water is said to be effective.

A fresh-water fish, *Barbus puckelli* is said to feed voraciously both on *Cyclops* and on the guinea-worm larvæ.

Diagnosis.—An intradermal test is said to have given positive results in 85 per cent. of cases.

... the affected

the skin she may be cut down upon, a broad tape passed round the centre of her body and gentle traction employed for her removal. Even if ... done in such a case. It is a different ... Then traction of ... gradual, carefully and intermittently performed, the worm being wound round a piece of ... the process abscess

specially likely to occur ... irritating contents into the subcutaneous tissues. This may take place before or after perforation of the skin has occurred.

muscular injections of an emulsion of the ... especially in the neighbourhood of the buried *Dracunculus* Extraction of the worm is said to be facilitated.

An injection of 1 in 1,000 adrenaline will relieve the prodromal urticaria immediately. The blister should be aspirated as early as possible so as to limit the size of the subsequent ulcer.

HEAT EFFECTS

A hot climate may damage health by its general effects, which are heatstroke or heat exhaustion, and by causing the local lesions prickly heat and sunburn. The general effects are the more immediately serious, the local lesions, though often regarded as minor disabilities, are nevertheless responsible for much discomfort and ill-health.

General Effects.—The unqualified term "Heat Effects" is used here to mean only the general effects. These may be brought about either by a very high atmospheric temperature or by a not-so-high temperature with a high relative humidity. Mild forms of illness due to heat may be encountered during the summer even in temperate countries like England. Serious heat effects may overtake men from time to time in most tropical and sub-tropical countries but the areas of their highest incidence, as far as the British soldier is concerned, are Iraq, Persia (Iran), and the borders of the Red Sea and the Persian Gulf.

It is important to distinguish between heatstroke, which is an acute febrile (usually hyperpyrexial) attack brought on by sudden failure of the heat-regulating mechanism of the body, and heat exhaustion, which is more an expression of derangement of body chemistry.

Etiology.—*Heatstroke* has been described as "a fever caused by climatic conditions in which the heat regulating mechanism fails to keep the body temperature below the normal upper limit" (Rogers and Megaw). Many experiments and much clinical observation go to prove that there is no mysterious quality in the sun's rays responsible for heatstroke. The stoker in the boiler room of a liner into which the sun's rays cannot penetrate may fall a victim. Those living high up in the hills in a tropical country, although nearer the sun, do not, owing to the comparative coolness at these higher altitudes, suffer from the effects of heat or fall victims to heatstroke, whilst those in the sweltering plains below may suffer severely.

In experiments in Manila, Aron found that monkeys exposed to a hot sun died within one or two hours. But if the animals were enclosed in large well-ventilated boxes with only the head exposed to the sun, they suffered no harm although the scalp temperature rose as high as 47° C.

Predisposing factors may conveniently be divided into external and internal.

External factors include high relative humidity, especially with air stagnation, unsuitable clothing and housing, and deficiency of fluid, food, or salt.

Internal factors are: pyrexia, *e.g.* from malaria or sandfly fever, gastro-intestinal upsets causing dehydration and salt-loss by vomiting or diarrhœa, fatigue and want of sleep; metabolic disturbances, especially from excess of alcohol, incomplete recovery from a previous attack, and in newcomers, lack of acclimatization.

Heat exhaustion is brought about by the same conditioning factors as heatstroke, but the symptoms are different because they are caused by disturbances of water- and salt-balance; failure of the heat-regulating mechanism, if it occurs, is a secondary and late event.

Symptoms.—Heatstroke and heat exhaustion require separate descriptions.

Heatstroke is always serious. The attack may be preceded for a day or two by prodromal symptoms which include defective sweating, exhaustion, giddine , headache, mental changes, anorexia, and frequency of micturition. The last is so unusual in very hot climates that it is an obvious warning. But the onset is often so sudden that an apparently healthy man may become unconscious in a few minutes. Hence the term "stroke".

In the developed attack the outstanding features are a burning, hot, dry skin and high fever, 105° to 109° F. The face is congested, the eye suffused, and the pulse full and bounding. Delirium, coma, and con vulsions may ensue. In coma the tendon and abdominal reflexes may be absent and the plantar reflexes extensor. Sometimes there are signs of focal damage in the central nervous system.

The cerebrospinal fluid is clear; its pressure is usually within normal limits, but occasionally it is raised and a pressure cone of the cerebellum has been seen at autopsy.

Urinary chlorides are usually normal or only slightly diminished and dehydration is absent.

Heat Exhaustion accounts for most of the cases of heat effects. It begins insidiously and seldom gives rise to anxiety unless exposure has been severe or treatment neglected.

In the common type the first symptoms are exhaustion, headache, anorexia, giddiness, nausea, pains in back and limbs, change in temperament, and mental confusion. Profuse sweating, pallor, and collapse characterize the next stage. Abdominal pain, vomiting, and cramps in muscles are common. On standing, the blood pressure falls and syncop is apt to occur; the pulse pressure is reduced. The skin temperature low but the rectal temperature may be raised to perhaps 101° F.

Chemically there is a salt-deficiency dehydration; plasma and blo chlorides are diminished, hæmoglobin and plasma protein are raised, ano blood urea is high. The urine is scanty and chlorides are either absent or present only in traces.

A mild attack may amount only to giddiness and faintness such as may overtake a heavily-laden soldier on the march in hot weather. In a severe case there are obvious signs of dehydration, sunken eyes, and inelastic skin. If this dehydration is not soon relieved the outlook may become grave indeed. Occasionally, after a week or ten days of increasing dehydration, there is a final phase of hyperpyrexia.

In Iraq and Persia, a notorious "heat-effects" area, another type of heat exhaustion has been described. Its incidence is mainly in the late and not necessarily the hottest part of the summer, whereas the usual typ occurs at the peaks of external temperature. Cases are characterized b defective sweating and polyuria, and the skin is always affected by prick

heat in the healing or desquamating stage. Vomiting, cramps, and cardiovascular abnormalities are not present. Mild pyrexia is usual. Chemically there is salt deficiency, but this is not gross and the patients are not dehydrated.

Differential Diagnosis.—*Heatstroke* may closely resemble cerebral malaria with high fever, or it may complicate malaria. If there is any doubt, the presence of malaria should be assumed, even though no parasites can be found in the blood. Every other cause of high fever with delirium, coma, or collapse must be considered, especially cerebrospinal fever, other forms of meningitis, and infective fevers. Cerebral hæmorrhage is differentiated by the fact that the rise of temperature, if present, usually follows the insensibility.

Heat exhaustion may resemble algid malaria, sea-sickness, acute alcoholism, and gastro-enteritis. Advanced or neglected cases may be confused with gastritis, peptic ulcer, intestinal obstruction and the pre-icteric stage of infective hepatitis. Frequency of micturition may suggest bladder disease. The mental symptoms may be wrongly attributed to purely psychiatric causes. In the last stages uræmia due to renal disease has to be differentiated.

It should be remembered that heat exhaustion often complicates other diseases.

In the common salt-deficient type of heat exhaustion an important sign is diminution of urinary chlorides. The following tests have been found useful:—

1. *Silver Nitrate*—a rough test. Take 5 c.cm. of the patient's urine in a test tube, add five drops of pure concentrated nitric acid and then a few drops of 1 per cent. solution of silver nitrate. Normally a thick curdy precipitate occurs; a slight haze or no change indicates that chlorides are absent.

2. *Potassium Chromate*—quantitative. *Requirements.*—A pipette and a test tube, a bottle (5 to 20 c.cm.) of 20 per cent. solution of potassium chromate (NOT bichromate), a bottle (20 c.cm.) of 2·9 per cent. solution of silver nitrate, distilled water.

Test.—To 10 drops of the patient's urine add 1 drop of the chromate solution—this gives a canary-yellow colour. Using the same pipette (washed with distilled water) drop in the silver nitrate solution, counting the drops. The end point is a sharp change in colour from yellow to brown.

Estimation.—The number of drops of silver nitrate solution used equals grams of sodium chloride for each litre of urine. (The number of drops × 100 equals mg. of sodium chloride per 100 c.cm.) For any but the roughest test the sample urine must be from a 24-hour specimen.

(*Note.*—Potassium chromate may contain sodium chloride as an impurity. A control with distilled water should, therefore, be done when fresh stocks are taken into use.)

Prognosis.—In *heatstroke* the duration of hyperpyrexia is the important factor. A temperature about 109° F. for a few hours is likely to be fatal Nevertheless, recovery from a temperature of 112° F. has been seen when treatment was instituted immediately. Serious features are persistent or relapsing high fever, prolonged unconsciousness, and circulatory failure.

In *heat exhaustion* recovery is the rule. In mild cases it is rapid Dehydration and salt deficiency are usually quickly remedied by treatment. It is only in the exceptional case in which dehydration is far advanced and of long duration that prognosis is bad. Late hyperpyrexia in these cases is very grave. The type of heat exhaustion with dysidrosis improves only slowly.

Prophylaxis.—Under war conditions this is often by no means easy. In the first place it is essential that due warning of the likelihood of the occurrence of heatstroke be obtained by the keeping of a careful watch on meteorological conditions. A wet-bulb temperature of 83° F. (28 4° C.) with little or no air movement represents the danger point.

Overloading of troops must be avoided, and as far as possible undue fatigue should be prevented.

glasses give comfort by protecting the eyes from the glare of the sun's rays.

Excessive exercise should not be indulged in, as the profuse sweating caused thereby, with consequent dehydration and chloride loss, may be the deciding factor in the production of heatstroke.

they cause

The men most likely to develop heatstroke are those who are unwell a healthy man in hard training can stand up to almost any climatic heat provided he has plenty of water; and precautions must not be such as to lower morale. It may be possible to establish water-points at centres of traffic and places where troops congregate, so that they can readily get cold drinks and a sluice down. Also, as loss of salt from the body as a result of excessive sweating is one of the main factors in the production of heatstroke, its replacement is necessary. This may be effected by the addition of salt to the drinking-water in the ratio of 10 grains of common salt to the pint of water. Care should also be taken that there is a sufficiency of salt in the ration, and it is best given with the meat ration when the men are most likely to take it. The main meal of the day should be taken in the evening during the hot weather.

In addition to camp and barrack heatstroke centres, and facilities for the treatment of this disease in hospitals, "heatstroke lorries" have been

designed to accompany convoys. Good facilities are needed at hospita[ls] in all hot countries, not only to treat incoming casualties, but also becaus[e] febrile patients in the wards are always liable to develop hyperpyrexia; they must be closely watched and immediately treated if deaths from this cause are to be avoided. Tented wards may be particularly hot, but can sometimes be cooled with wet brushwood screens or with fans. In hot weather, operations and anæsthetics should be reduced to a minimum. Certain drugs such as atropine (hinders sweating), strychnine (convulsant), thyroid preparations (increase metabolism), and opium are best avoided or reduced to a minimum.

There are individuals with a constitutional inability to sweat. These may have to be retained in hospital throughout the hot season, or, better, sent to the hills until the onset of the cool weather.

Acclimatization is perhaps the most valuable prophylactic measure. It includes not only the physical seasoning of the individual but also experience of unit commanders and men in common sense precautions. The process consists of strictly-controlled gradually increasing periods of work in the heat, and takes three to four weeks to complete.

Adequate fluid intake is essential. The minimum requirement is about 12 pints a day, men doing hard manual work need very much more.

Meals must be adequate in quantity and a good standard of cooking and service should be maintained.

Treatment.—In general the most important measures are provision of a cool atmosphere, rest, reduction of unduly high body-temperature, and correction of fluid- and salt-deficit.

Heatstroke.—The urgent necessity is to reduce the body temperature below the danger point as soon as possible. The patient should be placed naked on a light mattress or permeable matting on an iron bedstead, charpoy, or stretcher, or on the floor if none of these is available, and sprayed with ice-cold water. At the same time evaporation must be ensured by electric- or hand fanning or by the natural wind. When water-supply is limited, sponging with cold water or covering the body with a wet sheet is effective provided the air current is maintained. These methods depend mainly on abstraction of heat from the body by evaporation. Evaporation of water at body-temperature carries away 0·59 calories per gram whereas melting of ice takes away only 0·08 calories per gram. Seventy grammes of water evaporated from the skin remove as much heat as 1,000 grammes of water used as an iced enema. Unfortunately, if the atmosphere is nearly saturated with moisture, as may occur in the Persian Gulf, evaporative methods fail, and then immersion in a bath of cold water—about 50° F. (10° C.)—may be employed.

These methods are drastic and require care in their use. Rectal temperature must be closely watched minute by minute and cooling discontinued when it has been reduced to a safe level, *e.g.*, from 109° to 104° F., or from 106° to 102° F. The patient should then be wrapped in a dry sheet, and fanning should be continued—the rectal temperature being observed at ten-minute intervals. If the temperature rises again, the treatment must be repeated. It is usually safe to remove the patient from the heatstroke centre to a cool ward within two or three hours. To

Prognosis.—In *heatstroke* the duration of hyperpyrexia is the important factor. A temperature about 109° F. for a few hours is likely to be fatal. Nevertheless, recovery from a temperature of 112° F. has been seen when treatment was instituted immediately. Serious features are persistent or *relapsing high fever, prolonged unconsciousness, and circulatory failure*

In *heat exhaustion* recovery is the rule. In mild cases it is rapid. Dehydration and salt deficiency are usually quickly remedied by treatment. It is only in the exceptional case in which dehydration is far advanced and of long duration that prognosis is bad. Late hyperpyrexia in these cases is very grave. The type of heat exhaustion with dysidrosis *improves only slowly.*

Prophylaxis.—Under war conditions this is often by no means easy. In the first place it is essential that due warning of the likelihood of the occurrence of heatstroke be obtained by the keeping of a careful watch on meteorological conditions. A wet-bulb temperature of 83° F. (28·4° C.) with little or no air movement represents the danger point.

Overloading of troops must be avoided, and as far as possible undue fatigue should be prevented.

Times of marching require careful consideration, and should be selected so that starts are made sufficiently early to avoid the main heat of the day and yet not too early to interfere unduly with sleep. A sufficiency of the [illegible] glasses give comfort by protecting the eyes from the glare of the sun's rays.

Excessive exercise should not be indulged in, as the profuse sweating caused thereby, with consequent dehydration and chloride loss, may be the deciding factor in the production of heatstroke. [illegible] they cause.

The men most likely to develop heatstroke are those who are unwell: a healthy man in hard training can stand up to almost any climatic heat provided he has plenty of water; and precautions must not be such as to lower morale. It may be possible to establish water-points at centres of traffic and places where troops congregate, so that they can readily get [illegible] sufficiency of salt in the ration, and it is best given with the meal ... when the men are most likely to take it. The main meal of the day should be taken in the evening during the hot weather.

In addition to camp and barrack heatstroke centres, and *facilities for the treatment of this disease in hospitals,* "heatstroke lorries" have been

designed to accompany convoys. Good facilities are needed at hospitals in all hot countries, not only to treat incoming casualties, but also because febrile patients in the wards are always liable to develop hyperpyrexia, they must be closely watched and immediately treated if deaths from this cause are to be avoided. Tented wards may be particularly hot, but can sometimes be cooled with wet brushwood screens or with fans. In hot weather, operations and anæsthetics should be reduced to a minimum. Certain drugs such as atropine (hinders sweating), strychnine (convulsant), thyroid preparations (increase metabolism), and opium are best avoided or reduced to a minimum.

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move a patient at this critical stage by ambulance during the heat of the day is highly dangerous unless the journey is very short. When a transfer to hospital is necessary, it is safer to retain the patient in the local heat-stroke centre *until the* cool of the evening.

Rubbing with ice and iced enemas are not recommended. Antipyretic drugs are valueless.

Venous congestion, as shown by cyanosis, con*vulsions*, and signs of ...monary œdema, *is* an indication for venesection (10 to 20 oz.) and ... f oxygen by mask. If these measures do not ... nen (bromethal) ... ia. ... is valueless ... s and it may ... It must, however, ... s is in doubt. cause a cerebellar pressu... when the ... be employed, *but* with great caution, when the ... Coramine may be

Atropine or strychnine must not be administered.

... if a respiratory stimulant is required.

... infusion of fluids depends on the degree of ... treated and the load ... ion may cause or aggravate pulmonary ... yrexia must be treated first.

As mentioned above, it is often very difficult *to* exclude malaria. If there is the slightest doubt, 8 to 10 grains of quinine must be given *intra*venously very slowly, it may be repeated in six hours.

Careful watch must be kept for a recurrence of the hyperpyrexia; this is a dangerous and not uncommon event.

Heat exhaustion.—Very mild cases may be treated in the unit. Rest in the shade, a liberal supply of salted drinking-water, and perhaps 48 hours' light duty will suffice.

More serious cases with cramps, vomiting, frequency of micturition, pyrexia, or clinical signs of dehydration need to be treated in a heatstroke centre or hospital. A cooled atmosphere is extremely important, not only for its influence in promoting comfort and rest, but also for its even greater therapeutic effect in preventing further loss of fluid. An average individual at rest ceases to sweat profusely when the external temperature falls below 84° F. (29° C.). The best temperature, therefore, in which to treat heat exhaustion is 78° to 80° F. (25·5° to 26·6° C.), and this is often easily attained by evaporative methods, even when air-conditioning is not available.

In order to replace water and salt already lost patients should be encouraged to drink a large quantity of fluid, and a fluid-balance chart should be kept. The optimum intake is 16 pints in the 24 hours. Suitable fluids are water containing 10 grains of sodium chloride to the pint, lemonade, and milky drinks. A light diet should be added and normal meals given as soon as appetite returns.

When dehydration is severe or vomiting persistent, fluid should be given intravenously. Five pints of isotonic glucose-saline by drip in thre[e] hours usually suffice, thereafter fluids can be taken by the mouth. Occa[...]

sionally, in very severe cases, intravenous administration has to be continued.

Improvement is shown by cessation of cramps and vomiting, increase in pulse volume, restoration of blood pressure, larger urinary output, and gain in weight.

After-treatment.—All patients should be placed in a quiet cool ward. If this is air-conditioned they need gradual reacclimatization before being transferred to non-cooled accommodation. Heatstroke cases may be treated as for concussion; sedatives such as phenobarbitone may be given as required.

Patients who have had only mild heat effects may return to light duty or spend a period at a convalescent depot, but those who have had heat-stroke or severe heat exhaustion need at least three weeks' careful treatment before they are fit to go about. After this they should be sent to a cool station, special precautions being observed on the journey, and they should not return to a heatstroke locality during the hot weather.

Local Effects.—These are prickly heat and sunburn.

Skin lesions severe enough to require admission to hospital are not uncommon effects of heat. Many resist treatment especially if they have been allowed to progress beyond the early stages.

Prickly Heat.—Prickly heat is nearly always the initial lesion, it may be complicated by such conditions as furunculosis, intertrigo, bullous impetigo, and hyperidrotic eczema.

Prickly heat starts with a transient erythema followed by an angry papular rash and some œdema of the skin. The papules are surmounted by a minute vesicle, these lesions are often seen best on the shoulders and back. If at this stage healing takes place, the affected areas become dry and begin to desquamate. Some staining of the skin about the shoulder and buttocks may be left.

During the acute stages sweating is little, if at all, diminished, but in the healing stage the skin is dry and apparently not sweating. Normal sweating may not be established for several weeks.

Acute prickly heat is often relieved, though seldom cured, by frequent applications of a powder consisting of starch, zinc oxide, boric acid, and sulphur in equal quantities. In the severe and generalized forms, bathing twice daily with potassium permanganate solution (1/4,000) brings improvement while all measures which aid evaporation of sweat from the skin are helpful in the acute phase.

Sunburn.—Severe sunburn is easily caused in Europeans fresh to the tropics by injudicious exposure of the bare skin to the direct rays of the sun, either from carelessness or in attempts at tanning. Sun rays through light cloud or reflected from water also cause burning.

Mild cases present an erythema which may be accompanied by slight fever if the area is extensive. Severe cases develop extensive blistering and considerable constitutional reaction. These burns are as susceptible to secondary infection as superficial burns from other cases and should be treated on the same lines.

Severe sunburn increases the susceptibility to general heat effects.

Tanning, when established, is a protection from the sun, but care is needed to ensure that the process is gradual and limited to short periods of exposure at the beginning. Application of oils and fats during exposure increases the burning.

INFECTIVE HEPATITIS

During both World Wars, 1914–18 and 1939–45, there have been widespread explosive epidemics of non-spirochætal jaundice. Similar extensive outbreaks were reported in earlier campaigns; but since these occurred before the discovery of the leptospiral nature of Weil's disease, their etiology is uncertain.

During the period between the two World Wars, catarrhal jaundice, as it was then called, was reported as of common occurrence in most parts of the world, its incidence varying from an occasional sporadic case, commonest among children, to explosive outbreaks of almost epidemic intensity. Such outbreaks, often limited to one unit or small area of a

[illegible]

hepatitis is almost certainly a virus infection.*

An illustrative outbreak

An explosive outbreak comprising some ten thousand cases occurred in the Middle East during the last four months of 1942. The main [illegible] of this outbreak were strikingly similar to the epidemic of "camp

[illegible]

[illegible] during late September 1942, among the [illegible]
[illegible] holding positions in
[illegible] It spread rapidly
[illegible] sing 8–9 per cent.
[illegible] Western Desert the
[illegible] Hospitals, especi-
[illegible] Malta, and Cyprus,
[illegible] tained at epidemic
[illegible]

and Italy.

* Since this book went to press MacCallum and Miles have reported successful transmission of the infection to rats on a protein-deficient diet (*Lancet* 1946 Jan 5, p 3)

In the early days of the outbreak there was a heavy incidence among individual units and formations but as the disease spread it also became more thinly distributed and a comprehensive survey in Syria and Cyprus showed that 478 cases were drawn from 208 different units.

Epidemiology.—The chain of infection in the early phases of the Alamein outbreak led observers to suggest that infective hepatitis, in its epidemic form, might be a "place disease"—that infection might depend more on visiting a locality where other cases had occurred than on case-to-case infection. This raised doubts if infective hepatitis was spread by droplet infection, as catarrhal jaundice had always been supposed to be spread. It was now asked whether insects, possibly biting- or non-biting flies, might act as vectors, and in view of the large number of unburied carcases in the vicinity of El Alamein, carcase flies were suggested. Up to the present, however, no insect vector has been incriminated and most authorities believe that insect transmission is unlikely

It has been noted that the spread of infection among patients in hospital and from patients to hospital staffs is rare Thus, in a New Zealand general hospital which admitted over two thousand cases of the disease from the New Zealand Division, only one nursing sister among the whole staff caught the infection, although the majority of patients arrived in the early and presumably highly-infectious stage of the disease. Throughout the 1942–43 epidemic in Syria, only one nursing sister contracted the disease

Successful passage of virus from patients in the early stage of the illness to human volunteers has been recorded on several occasions, although the possibility of a naturally-acquired infection in the recipients could not be altogether excluded in at least some of the alleged "takes".

Incidence in different groups.—During the El Alamein outbreak (and at other times), it has been noted that in most units, especially in forward areas, an unduly high proportion of officers has been attacked. This has been a feature of the epidemic disease throughout the Middle East and North Africa and has been much commented on, but there have been some notable exceptions. The heavily-infected New Zealand Division reported no such tendency, nor was there any such "class distinction" either in the Royal Navy or in the American Army. In the Royal Air Force, flying crews, commissioned or non-commissioned, suffered more heavily than ground staff

Various hypotheses, none of them entirely satisfactory, have been advanced in explanation of this undoubtedly high officer-morbidity. In officers' messes, it has been suggested, there is a relatively generous consumption of alcohol and hygiene is faulty, especially with regard to washing facilities for table-crockery, both have been put forward as possible contributory causes No firm evidence in support of these suggestions has been forthcoming, and in Syria it was found that nearly one-third of the patients were teetotallers but that many escaped infection who were not by any means in that category.

Some dark-skinned races have appeared to be relatively immune to infective hepatitis Thus, the incidence among Indian sepoys was less than one-tenth of that among white troops in the vicinity; similarly,

Maoris who were in the line at Alamein alongside heavily-infected New Zealand troops escaped very lightly. The same relative immunity, suggested as being due to childhood infections, was noticed among the coloured troops of the Union Defence Force (South Africa) and of the American Army. The incidence of hepatitis was also relatively low among Maltese and Cypriots. On the other hand, a brigade of native troops from the Belgian Congo suffered heavily and had a relatively high mortality from this cause. Later, the incidence of infective hepatitis among native Indian troops in India and Burma was about one-third of that among British troops in the same theatre of war.

Symptoms.—The incubation period is considered by most authorities to be fairly constant at just over a month, the limits lying between eleven days and two months. Only a small proportion (2·5 per cent.) gave a history of previous jaundice.

Two main modes of onset are noted during epidemic periods. The first, and most common, has a short pre-icteric febrile phase lasting two to six days, not to be distinguished at this early stage from other short fevers. Anorexia and an enlarged and tender liver are fairly constant early signs; the anorexia is a specially useful sign. In some cases the initial fever may be fairly sharp (temperature 103°–104° F.) and the patient may complain of shivering, although a definite rigor is uncommon except in cases complicated by malaria. An early leucopænia with relative lymphocytosis is often noted. Direct evidence of jaundice is usually lacking at this early stage, but an excess of urobilin in the urine is common. The initial fever lasted five days or less in 85 per cent. of one large series.

[illegible]

jaundice.

It has been constantly noted that as soon as jaundice appears the patient regains his normal spirits; his appetite returns, and may indeed become voracious, and the stools become bile-stained. It is considered that the patient ceases to be infectious at about this stage.

[illegible]

presenting symptoms. Low fever may or may not be present in the early stages. Dark urine, pale stools, and increasing jaundice follow in rapid sequence.

In a small minority constitutional symptoms are entirely lacking and the patient's first intimation that anything is wrong is when he finds out for himself or his friends tell him that he is becoming yellow.

In an unknown but probably considerable proportion of cases the disease appears to abort at the termination of the febrile pre-icteric stage and jaundice fails to appear although the icteric index is usually somewhat raised and the urine contains excess of urobilin if not bile. These

cases of "inapparent jaundice" many of which, of course, are not diagnosed, raise points of epidemiological importance since they are probably just as infectious as those with clinical jaundice.

Whatever the mode of onset the course of the disease is almost invariably mild and benign although the icterus may take some considerable time to disappear completely.

It is stressed that anorexia is the most constant early presenting symptom whatever the mode of onset, it was noted as a prominent symptom in 93 8 per cent of a large series observed Vomiting or nausea, or both, occur in about one-quarter of the cases Abdominal pain and discomfort, sometimes quite late in the course of the disease, were noted in about one-third of the large group already mentioned The liver, usually enlarged and tender from an early stage, soon loses its tenderness but may remain considerably enlarged far into convalescence and in a few cases the lower border may remain permanently palpable well below the costal margin In the same large group of cases the incidence of splenomegaly was about 25 per cent, but this is a variable feature The average stay in hospital for this group was 33 days with extremes of 11 and 100 days, the appetite returned on an average on the ninth day after the onset and the patient got up on the nineteenth day

Although the depth of jaundice varies greatly, relatively few even of the deeply-jaundiced patients suffer much inconvenience from pruritus.

Transient nephritis with gross albuminuria and cylindruria is relatively common among the more deeply-jaundiced patients The urine usually becomes free from bile about the fourteenth day—long before the patient loses his icterus

Liver biopsies, undertaken in a limited number of patients whose attacks of epidemic infective hepatitis appeared to be running a normal course, showed periportal fibrosis with reticulosis in the centre of the lobule.

Complications.—Complications of any importance are rare.

As already noted, transient nephritis, perhaps due to chemical irritation by the bile during excretion, occurs in a proportion of the more deeply-jaundiced cases

A morbilliform eruption has been reported in a few cases

Colic, occasionally severe enough to mimic an acute surgical emergency, has been noted in a few patients, in some, this has been due to hæmorrhagic collections either in the deep muscles covering the abdomen or in a viscus, in others, the etiology has been obscure Very occasionally, acute appendicitis or biliary colic may be closely mimicked by an overlying ingravescent hæmatoma Other hæmorrhagic complications are rare, but they include hæmaturia, epistaxis purpura, and bleeding gums.

Evidence of meningeal irritation was noted in one small series on the Burma front.

Liver insufficiency —In a very small proportion of cases (between 0 2 and 0 5 per cent in white troops and up to 1 5 per cent in Indian and African native troops) evidence of acute liver insufficiency has suddenly appeared "out of the blue", usually in a case in which the onset and clinical course up to the appearance of these alarming symptoms had given

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In a few instances the evidence of hepatic insufficiency has ... s
dramatic, cholæmic symptoms have been less marked, and the patient has suffered from prolonged hectic fever, progressive emaciation, and ... eventually died from sub-acute liver necrosis or ... protracted illness.
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seen only when very large numbers come under review. *The normal course of the disease is quite uneventful, if somewhat prolonged,* the patient suffering no apparent ill-effect.

Relapses occur in about 5–8 per cent. of cases. Opinions differ about ... whether the length of stay in bed has any direct bearing on the tendency ... such relationship and recommends getting ... their appetite has

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extending over many months.

Diagnosis.—The disease presents great diagnostic difficulties in the pre-icteric stage and in mild cases which fail to develop clinical icterus.

Cullinan has used the *histamine test* with success in these early or abortive cases.

Histamine skin test.—Select an area of skin free from sunburn and freckles Clean the area Inject intradermally 0 1 mg. of histamine dissolved in 2 0 minims of 1/20,000 solution of merthiolate in water. A white wheal forms surrounded by a zone of erythema. The wheal is examined at the end of three minutes by stretching it between the thumbs in *good daylight* and comparing the colour of the centre with the colour of the normal skin outside the erythematous zone

Demonstration of bile pigments in the urine is extremely simple and of great value, though not completely diagnostic.

Differential Diagnosis.—In the febrile pre-icteric stage clinical diagnosis from other short-term fevers (*e g* malaria, sandfly fever, dengue, influenza) is often impossible Malaria and epidemic hepatitis may co-exist in the same patient, and jaundice is a not uncommon complication of subtertian (*P. falciparum*) malaria (bilious remittent fever). In Sicily, where a wave of subtertian malaria complicated by jaundice ran concurrently with an epidemic of infective hepatitis, the differential diagnosis became exceedingly difficult and mistakes were inevitable.

Weil's disease may closely resemble infective hepatitis and it is only since the discovery of *Leptospira icterohæmorrhagiæ* (1915) that these two diseases have been separated Polymorphonuclear leucocytosis, a hæmorrhagic tendency, conjunctivitis, severe muscle pains, and nephritis are very constant and important clinical pointers to Weil's disease. Leptospiræ may be cultured from the blood in the first five days of the disease or demonstrated in the urine in the third week or later, but both these procedures need skill and experience and false-positive reports are often the outcome of failure to recognize artefacts. The most simple method of making the diagnosis of Weil's disease is to submit two or more samples of serum—one before and one after the tenth day of illness—to a laboratory which is equipped to carry out one of the serological methods of diagnosis

Jaundice is not uncommon in enteric infections, especially paratyphoid C

Jaundice from the arsenical treatment of syphilis and the injection of homologous serum may present diagnostic difficulties unless the possibility is remembered and a history forthcoming

Prophylaxis.—This cannot be satisfactory until both the cause and epidemiology of infective hepatitis are fully worked out.

There is reason to believe that spread is normally by droplet infection especially between epidemic periods. There is also convincing evidence, both from America and Britain, that the virus of infective hepatitis remains viable (for how long is unknown) in the fæces of patients in the early stages of the disease Voegt and Findlay have both claimed that volunteers can be infected by ingestion of human urine. Spread by fæcal and urinary contamination is therefore a possibility that must be taken account of. It fits in with a recent suggestion, supported by evidence from American sources, that the disease may be water-borne, especially

in epidemic periods A further and somewhat disquieting recent discovery is that the virus or other agent responsible is peculiarly resistant to chlorination or even super-chlorination of water.

prevention and control of droplet and fæcal infections, remembering the possibility that the virus may be carried by water and is resistant to chlorination. Especially in epidemic periods, his measures should include the segregation of patients suffering from infective hepatitis.

Treatment.—No satisfactory specific treatment for infective hepatitis has yet been evolved. The use of methionine and other sulphur-containing amino-acids gave rise to early hopes, largely based on experimental data, that liver damage might thus be limited or prevented These hopes have not been realized.

Treatment with choline, a known lipotropic agent, has not been more successful. Interesting work in America shows that treatment with human gamma-globulin during the incubation period may prevent development of the disease

Patients with infective hepatitis are best nursed in special wards on

with only slight (if any) fat restrictions and plenty of carbohydrate and *protein of high biological value can be given.* There appears to be no

doses of insulin have appeared to influence the course in a few cases, for lack of anything better, they are probably worth trying.

Sulphonamides and penicillin have no place in the treatment of this disease.

[illegible] on how long the patient should be kept in bed. Some

recovered his appetite and sense of well-being. The cautious [illegible] that the incidence of relapses and of late complications is increased if the patient is allowed up too early; the others maintain that there is no evidence in support of this, and insist that due care is better than excessive care.

Post-Arsenical and Homologous Serum Jaundice.—The war of 1939–45 brought an increasing incidence of jaundice from both causes, especially from inoculation of organic arsenical compounds (arsphenamine, mapharside, etc.), in the treatment of syphilis

Authoritative opinion now holds the view that post-arsenical jaundice was caused by the introduction, by way of an imperfectly-sterilized syringe or needle, of blood or serum containing a minute trace of the virus of infective hepatitis or some allied icterogenic agent. Special precautions were accordingly taken in the sterilization of needles and syringes between individual injections and the incidence of jaundice from this cause was appreciably diminished. Syringes and needles used for venepuncture need equal care for the same reason.

Post-arsenical jaundice closely resembles infective hepatitis. The onset is usually insidious rather than acute and febrile, and the course of the disease is more severe and prolonged than in ordinary infective hepatitis. Complications (especially ascites and cirrhosis) are also more frequent. As in infective hepatitis, the most common cause of death is acute liver necrosis, the mortality from this cause being considerably higher than in infective hepatitis.

A relatively high incidence of jaundice was also noted during the 1939–45 war following the injection of certain products containing human serum, notably yellow-fever vaccine. The incubation period of this homologous serum jaundice is considerably longer than that of infective hepatitis, averaging 60 to 90 days instead of about a month. Only a few batches of yellow-fever vaccine have been icterogenic but the long incubation period of the jaundice has led to their being widely used before their harmful nature had disclosed itself.

It is practically certain that infective hepatitis virus or some allied icterogenic agent was introduced as a contaminant by the pooled human serum used as a constituent of former batches of vaccine. Human serum has now been eliminated from the manufacture of yellow-fever vaccine and there has not since then been any jaundice from this cause. At one stage, this post-yellow-fever-vaccine jaundice was a serious problem, especially in the U.S. Army.

Jaundice may follow the use of other products which contain human serum—for example, mumps and measles convalescent serum and dried plasma—and it may follow blood transfusion. The risk is greatest with pooled sera, and when only traces of serum are involved—as in syringes contaminated by venepuncture. This, it is suggested, is because in the healthy but icterogenic donor, the icterogenic agent is held in check by neutralizing substances. These are diluted by pooling, but a minute dose of the icterogenic agent is infective, therefore a trace of serum from an icterogenic donor may be more dangerous than a pint of his blood.

The post-mortem and biopsy appearances of the liver in all varieties of homologous serum jaundice are identical with those of infective hepatitis and post-arsenical jaundice. But this does not prove that only one infective agent is involved. It remains for further work to show whether the different types of disease, with their different incubation periods, are caused by one agent gaining access to the body by different routes, or by two distinctive agents. On the whole, opinion and evidence favour the view that the two clinical entities have separate causative agents.

LEISHMANIASIS

Under the heading of *Leishmaniasis* two diseases are included whose clinical pictures are very different :—

1. Visceral leishmaniasis (kala azar).—Several entities can be recognized :—
   Indian kala azar
   Mediterranean kala azar (often incorrectly called infantile kala azar)
   Sudanese kala azar
2. [illegible]

(Espundia, Uta).

Although visceral and cutaneous leishmaniasis are diseases *with widely-divergent* clinical pictures and markedly-contrasted *prognosis and although* the two rarely co-exist in the same area, visceral leishmaniasis is occasionally followed by a dermal form of the disease known as post-visceral dermal leishmaniasis. This is entirely distinct from, and *not to* be confused with, true cutaneous leishmaniasis, which *it does not resemble.* Kala azar and true cutaneous leishmaniasis *may rarely co-exist in the* same patient.

No morphological differences have been found between *Leishmania donovani*, the causative agent of the visceral disease, and *L. tropica* and *L. braziliensis*, which are responsible for the cutaneous and muco-cutaneous forms.

It is now beyond reasonable doubt that species of *Phlebotomus* act as vectors, as far as we know, they are the sole vectors of *all varieties of* leishmaniasis.

Kala Azar

Visceral leishmaniasis may be expected among *individuals* who have lived in or visited endemic foci of *the disease. Thus, it is common among* Indian *troops*, especially Gurkhas and other *races recruited from* North-East India. *The* incidence in Bengal and Assam *is especially high.*

During the Abyssinian campaign (1941) a particularly fatal variety of the disease was seen among both British and native troops stationed *in* certain districts of Eastern Sudan, *especially the districts* of Gedaref and Gallabat, near the Abyssinian border. East African troops stationed round the northern end of Lake Rudolph in N. Kenya also suffered heavily.

In the later years of the 1939–45 war there were many cases of Mediterranean kala azar among troops scattered along the North African coast and in other endemic foci of the disease *along* the Mediterranean littoral such as Sicily, Southern Italy, Greece, and Crete. As in the war of 1914–18, a few indigenous cases were reported from Malta.

Etiology.—The disease is due to a protozoal parasite, *Leishmania donovani*. It is one of the flagellates, but in man occurs solely as a small

ovoid or sometimes nearly spherical organism which, when stained, shows two masses of chromatin, the larger, a nucleus, placed either centrally or peripherally, the smaller, a very definite short rod or dot, the kinetoplast* (Plate 20). It usually stains more deeply than the nucleus. The cytoplasm of the Leishman bodies is often vacuolated. They multiply by fission and may be found crowded together in endothelial cells. Their chief habitat appears to be the endothelial cells of blood-vessels and lymphatics, especially those of the spleen, the liver, the bone marrow, and the skin. They also occur in the blood, inhabiting both the mononuclear and polymorphonuclear leucocytes.

If cultures are made in appropriate media flagellate forms of the parasite develop. The forms in the human body are resting stages of the parasite, while the cultural forms are analogous to those which occur in the insect vector of the disease.

There is now no reasonable doubt that the vector of all these closely-related varieties of visceral leishmaniasis is the sandfly *Phlebotomus*. In fact, transmission of Indian kala-azar by the bite of *P. argentipes* has been proved experimentally. Parasites ingested by these sandflies rapidly become transformed into flagellates which, by rapid multiplication, fill the anterior part of the stomach and extend into the pharynx, buccal cavity, and proboscis. In some cases animals (hamsters) have been infected by the bites of experimentally-infected flies. In India the vector is *P. argentipes*, in the Mediterranean region *P. perniciosus*, and in North China *P. chinensis*. Though viable parasites may escape from ulcers in the intestine, bladder, and naso-pharynx of infected individuals, it is very doubtful if this brings about transmission except possibly on a very small scale, although hamsters have been experimentally infected by the oral route.†

Symptoms.—The disease may have a sharp onset, or may begin indefinitely. In the former type of case, the initial fever may suggest enteric, though usually there is not the same degree of prostration as in that infection, and the tongue remains clean and the appetite good. Or, the fever may be intermittent, and if it is accompanied by rigors malaria is simulated.

Again, the onset may be insidious, and in such instances a patient with a history of a few days' illness may show enlargement of the spleen indicative of an infection of several months' duration.

Whatever form the fever assumes, its most characteristic feature is a double remission in the twenty-four hours. This is often evident on a four-hourly chart, but in doubtful cases three-hourly records should be kept. After the usual morning drop, the temperature remains low until the middle of the day, and then rises during the afternoon. Towards evening it drops, but rises again during the night, and falls towards morn-

* This is the term originally applied by Alexeieff to the corresponding body in *Bodo*. As Wenyon points out, there is no evidence that the structure is a nucleus.

† Leishmania will develop to the flagellate stage in the body of the bed-bug under experimental conditions, but there is no evidence to show that this insect transmits leishmaniasis under natural conditions.

ing. This tendency to a double rise in the 24 hours, is very characteristic of the disease and it is seen at some stage in about 60 per cent. of cases. But it is wrong to suppose that a double rise will show itself on every day of the disease. On the contrary one may have to watch the 4-hourly chart carefully for many weeks before a typical example is seen. When they occur, the double or even triple daily rises tend to be grouped in series, occurring every day or every other day for a week or more, and then being entirely absent for weeks or even months.

During the 1939-45 war the Mediterranean cases were less acute in their onset and course than those from the Sudan. In the Mediterranean

to occur in the early morning or forenoon), were often a feature. Some cases were found to have high fever with minimal symptoms on first reporting sick.

After some two to six weeks of fever, a period of complete or partial

relapse.

In the average case of kala-azar the spleen is usually easily palpable after the first month or so, but in some cases, especially of the rapidly-fatal Sudanese form, the organ may be difficult to palpate, although a subsequent autopsy may show that it is considerably enlarged. Clinical enlargement of the liver is less constant. The spleen enlarges more rapidly (and is not so hard and therefore less easy to palpate) than the spleen of chronic malaria. At first the spleen and liver may return to their normal size during an apyrexial interval, but eventually the enlargement becomes permanent. It has been pointed out that the spleen takes about one month to reach the costal margin, and enlarges approximately at the rate of one inch a month, so that a spleen two inches below the costal margin indicates an infection probably of three months' duration. Occasionally the liver is more markedly involved than the spleen. The blood shows a marked leucopenia, the decrease chiefly affecting the polymorphonuclears, with a relative increase of the lymphocytes. In a differential blood count, probably no eosinophiles will be seen unless there is a superadded worm infestation, in which case the eosinophile count usually rises to that of a normal person. Within a month of onset some appreciable drop in the white count is to be expected. Later, counts of about 2,000 per c.mm. are common, and in advanced cases the white cells may be reduced to 1,000. There is an accompanying anæmia, relatively less marked than the leucopenia, and the proportion of white and red cells may be 1 : 1,200 or 1 : 1,500 instead of the normal 1 : 600. The degree of anæmia is variable. While less constant and not so characteristic as the leucopenia severe grades of secondary anæmia sometimes occur but these are often found in cases complicated by malaria. The colour index is not affected.

As the disease progresses, various symptoms may manifest themselves,

grey colour of the skin, with pigmented areas surrounding the mouth, on the forehead, temples, etc, is very striking.

In untreated cases the condition drags on its weary course for months and even years, becoming eventually a low continuous fever, or the patient dies from exhaustion or some intercurrent malady such as pneumonia or cancrum oris.

Complications.—Phthisis, pneumonia, cancrum oris and other septic infections, diarrhœa and dysenteric symptoms may be mentioned. Persistent cough is not uncommon. Most of the septic complications, including cancrum oris, appear to be consequent on the marked neutropenia and therefore tend to occur relatively late in the disease.

Sometimes during treatment there is marked enlargement either of the lymphatic glands generally or of the abdominal glands alone. They usually disappear when further suitable treatment is given.

Occasionally *L. donovani* gives rise to non-ulcerative papillomatous nodules of the skin. These have been noted in persons who have undergone treatment for kala-azar, and at a time when they appear to be free from any visceral involvement. Cases of kala-azar with skin involvement have been noted with special frequency in Northern Sudan, where, in one series investigated, the organism was isolated from various skin lesions in more than 50 per cent. of cases. As a result of the relative frequency of the skin involvement and infrequency of the organisms in the peripheral blood it has been suggested that, in this area, infection has probably occurred *via* the skin, and not the blood. Gland punctures, which were positive in every case in the above series, support the above hypothesis.

In marked cases of the nodular type of post-kala-azar dermal leishmaniasis affecting the face the differential diagnosis from leprosy may present difficulties.

Diagnosis.—The long-continued and completely irregular fever, with or without the characteristic double rise, increasing splenomegaly, and marked and progressive leucopenia, combine to produce a very typical picture which becomes all the clearer if the patient is known to have been domiciled in or to have visited an endemic area of kala-azar. But the diagnosis can be made with certainty only by the discovery of the parasite, either in the peripheral blood, in spleen juice obtained by puncture, or by the newer sternal or lymph-node puncture. These are safer proceedings than spleen puncture, but of less diagnostic value (of one series examined by Napier 75 per cent. were positive by sternal puncture, 90.8 per cent. by splenic puncture). On the whole, gland puncture has given disappointing results, and in many cases, including advanced cases, glands have not been found which were prominent enough to puncture. Sternal puncture should, in view of its relative safety, always be done first, if negative, splenic puncture may then be performed with the usual precautions.

Sternal puncture can conveniently be performed with a Salah needle

introduced with aseptic precautions under procaine anæsthesia. The needle may be inserted over the lower end of the manubrium sterni. On striking the bone it is directed towards the patient's head at an angle of 30 degrees to the surface of the bone and is bored in with a semi-rotatory motion. When the needle has entered the marrow cavity the stylet is withdrawn and 0 25 c.cm. of marrow fluid is sucked out with a dry syringe This fluid, which looks like blood may be expelled into a small tube containing potassium oxalate (2–3 mg. per c cm.). The needle is removed and the puncture wound sealed with collodion. A wide-bore flat-bevel lumbar-puncture needle is sometimes employed instead of a Salah needle, but it should be provided with a guard to prevent the possibility of its puncturing the heart by penetrating beyond the posterior border of the sternum. Death has resulted from this accident.

Splenic puncture gives good results, but is not wholly free from danger. With proper technique and due precautions it is a perfectly justifiable procedure, but it should never be undertaken until a blood examination has been made and all chance of leukæmia excluded. An ordinary all-glass 2–5 c cm. syringe with a clean sharp needle 1¼ inches long will ... required the syringe should be ...

puncture and no safer.

... search for parasites ... looks at it the ... apparent.

... media ... water ... ative, ... being ... blood ... uipped ... es may ... scopic

examination, and such cultures may show flagellates when no organisms were found in the spleen smears. Successful cultures have also been obtained from the urine.

The aldehyde test, carried out as follows, is often useful About 5 c cm of blood are withdrawn from a vein and allowed to stand until the serum separates To 1 c cm. of the serum in a test tube one drop of freshly-prepared commercial formalin is added, the tube well shaken and placed in a rack at room temperature. "If the blood is from a well-established case of kala-azar, three to four months or more, the serum will immediately become viscid, within a minute or two will have 'set' so that the tube can be inverted without the serum being spilled. . . . Within three to twenty minutes, the time varying in different cases, the whole of the serum will have become absolutely solid and opaque, like serum coagulated by heat or the white of a hard-boiled egg. . . ."

Although helpful, the result of the test is not conclusive A negative reaction by no means excludes the disease.

Diseases other than well-established kala-azar (three to four months duration, or more) may cause a doubtful serum reaction, the most important of these being advanced tuberculosis and leprosy, but Napier and Muir state that in these conditions the serum is never both solid and completely opaque. The test may also be positive in trypanosomiasis.

Chopra's antimony test is said to be more delicate than the aldehyde test and appears somewhat earlier in the disease (two months after onset).

The test is carried out as follows: The serum from 1 c.cm of venous blood is diluted with ten times its volume of doubly-distilled water and placed in a miniature test tube, a 4 per cent. solution of urea stibamine is then run slowly down the sides of the test tube with a clean capillary pipette. A positive result is shown by a heavy flocculent precipitate forming immediately, this settled as a flocculent mass in half an hour. A fine granular precipitate which settles more slowly, but forms a compact mass at the bottom of the test tube, denotes a doubtful positive. No precipitate denotes a negative result

Neither the aldehyde test nor Chopra's antimony test are of proved value in the differential diagnosis of the Sudan variety of kala-azar. The former is often negative in established cases of the disease and is frequently positive in Egyptian splenomegaly

Differential Diagnosis.—Leukæmia, chronic malaria, tuberculosis, Banti's disease, and idiopathic tropical splenomegaly are the conditions most likely to be confounded with kala-azar, but in certain places undulant fever, trypanosomiasis, and schistosomiasis with enlarged spleen have to be excluded In the early stages it may be confused with typhoid or paratyphoid and, when more advanced, with abdominal tuberculosis or malignant disease. It must be remembered that the disease may occur along with malaria

Prognosis.—Until quite recently this was distinctly bad, although the disease was by no means invariably fatal. The introduction of antimony has, however, greatly altered the outlook

Prophylaxis.— As far as epidemic kala-azar is concerned, experience

has shown that it should be treated like any other communicable disease by isolation of the sick, disinfection or destruction of dwellings and fomites, the inculcation of cleanliness both domestic and personal, the improvement of housing conditions, with, as special measures, removal to a new site and the destruction of infected animals such as dogs.

In endemic regions precautions should be taken to guard against the bites of *Phlebotomus*, and the breeding places of these insects located and attacked. (*See* Arthopod pests and Appendix I.)

Treatment.—The established treatment for kala-azar is intravenous administration of antimony, most effectively as one of the pentavalent compounds such as Neostibosan (von Heyden 693), Stibosan, urea- and carbo-stibamine, and stibamine glucoside (Neostam). *The preparation*

is more likely to experience unpleasant sensations during and after the

injections should be given and the course may be repeated after one month if necessary.

intramuscular injection. The dose varies from 2 c.cm. to [illegible] c.cm., given on alternate days.

Children are tolerant of antimony. For Stibosan the following dosage is recommended: One-and-a-half to three years, 0 1 g.; six years, 0·15 g.; fourteen years, 0 25 g. If intravenous medication is impossible, Stibosan may be given in 0 1 g. doses into the gluteal muscles (not subcutaneously) in a 5 per cent. solution. *Some pain is to be expected, and for this reason injections* should not be repeated at the same spot. Reaction after *injection* is an indication for reduction of dose.

Before the introduction of the more effective pentavalent compounds, sodium antimony tartrate was relied on for treatment, and is still sometimes employed.

In the Sudan variety, which does not react to antimony, and in the *promising results have been*

744). This drug

5 to 2 6 *mg. per kilo* body weight by the intravenous route. A course of fifteen injections of 2 *mg. per kilo* has been given, repeated after seven days' interval if necessary. The solution should be freshly prepared in distilled water

made up to a strength of 10 mg per c cm. without heating and administered slowly. Thrombosis of veins is much reduced if the drug is dissolved in 50–100 c cm. of distilled water.

Even the most desperately ill patient may respond to this treatment; but toxic effects are more serious than was at first supposed. The minor symptoms, such as transient loss of consciousness, flushing, nausea, headache, increase in pulse-rate, and sweating, usually pass off in a short time. But there are now reports of delayed toxic manifestations, including peripheral neuritis and fatal hepatitis and pancreatitis, appearing after the patient has recovered from the disease In many of these cases the solution had not been freshly prepared. Intractable trigeminal neuralgia, usually bilateral, is unfortunately a not uncommon sequel of the stilbamidine treatment of kala-azar. In at least one case the severity of the pain drove the patient to an attempt at suicide Various paræsthesiæ, often described as like a red-hot or electric needle shooting in beneath the skin, and usually localized over the butterfly area of the face, may precede, accompany, or replace the tic douloureux It is so far impossible to predict the case that will be affected or to define the circumstances in which this distressing complication of stilbamidine treatment is likely to occur Although in some cases the dosage has been excessive in others it has been well within therapeutic limits.

For this reason and in spite of its undoubted efficacy in the treatment of kala-azar, stilbamidine (M & B 744) is now reserved for the relatively few cases, especially of the rapidly-fatal Sudanese variety, which fail to respond to antimony.

It is now suggested that the drug should be given less intensively—*e g* on alternate days for not more than a fortnight, followed by an interval of at least a fortnight before starting another course

The patient's general treatment must not be forgotten, and a nourishing and well-balanced diet is required, together with such tonics as may be indicated.

CUTANEOUS LEISHMANIASIS

(Oriental sore)

This condition—once known as Oriental sore—is better termed cutaneous leishmaniasis, for the lesion is not confined to Oriental regions nor is it always an open sore. Cutaneous leishmaniasis is essentially a disease of animals which is communicable to man It is endemic in certain well-defined and widely-distributed areas, epidemics have been reported.

The causal organism is the protozoon *Leishmania tropica*, infection with which is almost always acquired through the agency of *Phlebotomus*. Sergent and others have caused oriental sore in a locality where the [illegible]

The infecting parasite of canine leishmaniasis, *L. canis*, is serologically identical with *L. tropica*, which causes the corresponding lesions in man

Moreover, there is a form of cutaneous leishmaniasis common to both dogs and men; experimentally, each can be infected from the other. Cats, monkeys, rats, mice, and guinea-pigs may also be infected with *L. tropica*, and according to Russian observers other important reservoir hosts of the infection are wild rodents (chiefly gerbils, sometimes jerboas) that live in burrows which they share with the sandfly vector. Experiments have shown that, under certain conditions, house flies can act as mechanical vectors of *L. tropica*, and it is possible they may sometimes infect open sores and wounds.

There is strong evidence that *Phlebotomus papatasii* and *P. sergenti* are vectors of cutaneous leishmaniasis in many parts of the Middle East. Some authorities consider the stable fly, *Stomoxys calcitrans* a likely carrier. The bed bug (*Cimex lectularius*) and, in South America, certain ticks have also been regarded as possible vectors.

Post-kala-azar dermal leishmaniasis occasionally follows successful treatment of the visceral disease.

Symptoms.—Russian work has differentiated two main types of the disease besides the muco-cutaneous form. The first, a chronic or "dry" type that lasts for 12 months or more, is prevalent in towns; the papules are present for some months before ulceration. The second, an acute or "moist" type that lasts less than six months, occurs in open country; the lesions ulcerate in a week or two or even in five to ten days. The following names have been suggested: "dry type"—*Leishmaniasis cutanea tarde exulcerans*; "wet type"—*Leishmaniasis cutanea cito exul-*

suggests what might be called an indolent mosquito bite. It is less

the lesions are heaped up and moist.

Sooner or later ulceration occurs (Plate 23), often as a result of an injury.

The ulcer is painless and may be an inch or more in diameter. The

surrounding tissue may become œdematous

granulations being replaced under the scab by healthy pink ones and the ulcer becoming shallower. Eventually a white or pink scar is left which may be very slightly depressed and is disfiguring; it closely resembles a vaccination scar.

It is said that the dry and wet types are immunologically distinct—each, if the attack is not rapidly aborted by treatment, conferring immunity against further infection with the same type but not against the other type. Vaccination has been attempted with live cultures of *Leishmania*, immunity takes about a year to develop and is complete only against the strain used for inoculation It is obvious that the assessment of such vaccines requires further study and it is unlikely that they have an important application in present conditions. It is of interest to note that Bagdad mothers inoculate their infants on the extremities with material from sores, their object being to prevent the development of unsightly scars on the face.

Various other clinical varieties may be encountered. In the keloid form the organism causes raised, shiny, softish, movable mounds of tissue covered by pinkish skin. These do not ulcerate, but resolve by a gradual shrinkage and drying. Or large heaped-up papillomatous masses may result, which may resolve, as in the keloid form, or break down and give rise to open sores. In South America the mucosæ of nose, mouth, and pharynx, as well as the skin, are attacked in some 10 to 20 per cent. of cases of cutaneous leishmaniasis. The resulting lesions spread extensively with great disfigurement and even danger to life. They may be rendered even more serious and repugnant by the entry of the larvæ of *Chrysomyia macellaria* and other myiasis-producing flies. The lesions are called by various local names such as "espundia" or "uta" (Peru), and "bubas" (Brazil); they differ from ordinary cutaneous leishmaniasis both in their greater severity and in that there is not any tendency to spontaneous cure.

Diagnosis.—This can only be made with certainty by the finding or cultivation of the specific parasite. The parasites may be found in pus from the ulcer surface, but are more readily discovered by puncture of the unulcerated margin (Plate 22).

Differential Diagnosis.—Cutaneous leishmaniasis must be distinguished from the so-called trench sores, desert sores, and other similar conditions. This can only be done with certainty by microscopic or cultural examination, but in desert sores the condition is more acute and less lasting than in the specific infection. Ulcus tropicum must also be distinguished. This is readily done with the microscope (*see* Skin Diseases), while classical oriental sore differs in never becoming phagedænic. Rodent ulcer and extra-genital chancre are other conditions which may simulate oriental sore. Certain forms of blastomycosis, leprosy, nasal myiasis, lymphogranuloma, and muco-cutaneous syphilis may also cause difficulties in diagnosis.

Treatment.—Intravenous injections of antimony tartrate, or of one of

the pentavalent compounds, as described in the section on kala-azar. This is the treatment of choice for multiple sores, or for those causing disfigurement or serious inconvenience. But, unfortunately, lesions on the face, and especially those on the nose, are the most likely to prove resistant to intravenous antimony. Usually from 8 to 15 grains of antimony tartrate will suffice and, as in kala-azar, the pentavalent compounds are more effective. These are given as described in the section on that disease.

Berberine sulphate.—For local therapy, a 1 to 2 per cent. solution of berberine sulphate may be injected into the base and infiltrated margin of the sore, two such injections are said to suffice. This painful procedure is seldom employed.

Mepacrine.—Mepacrine has also been used, it is less painful than berberine sulphate and seems to give just as good results. One or two 0·1 g. tablets are dissolved in 5 c cm. of warm water (2–4 per cent. solution) which is allowed to cool to 37° C. before being used to destroy early papules by infiltration at several points. In the ulcerating phase the sore is treated by infiltration with up to 10 c cm of 3 per cent. solution or application of 10 per cent. ointment. Complete success is not claimed for any of these methods.

Applications of carbon dioxide snow applied for 5–30 seconds every ten days have also given good results.

The older methods of treatment by scraping or excision, or by application of caustics such as permanganate of potash in fine powder, have [illegible]

[illegible]
type of treatment must be observed [illegible] resists all known [illegible] to self- [illegible] buted to whatever treatment chances to coincide [illegible] process of resolution [illegible]

Prophylaxis.—Paint the site of all fly and other insect bites with iodine as soon as possible. Warn against the danger of infection by personal contact and that of auto-infection by scratching. Take appropriate

measures against sandflies (*Phlebotomus*). (*See* under Arthropod Pests and Appendix I.)

LEPROSY

From historic times leprosy has been a much-dreaded infection because of the disfiguring deformities associated with its late stages, and the rigid segregation formerly enforced upon its unfortunate victims. Today, social measures and advances in treatment have done much to improve the outlook. But the disease is a serious one, and the word "leper", which enlightened workers wish to abandon, carries a grave stigma. Therefore, it is important that medical officers in the tropics should know enough about the disease to enable them both to make an early diagnosis when the evidence is there, and to avoid all mention of leprosy when there is no justification for suspecting the disease.

Leprosy is a chronic, slowly-progressive infection affecting mainly, although not exclusively, the skin and nerves. It is caused by an acid-fast organism, *Bacillus (Mycobacterium) lepræ*, which was first described by Hansen in 1871.

Geographical distribution.—The heaviest incidence of the disease is in India, China, and tropical Africa. But it is found also in Japan, Burma, Indo-China, Thailand, Malaya, the Philippines, East Indies, and Pacific Isles. It is not uncommon in Egypt, South Africa, Madagascar, Central America, along the North coast of South America, and in some of the West Indies.

In Europe, indigenous cases occur in Iceland, Norway, Sweden, the Baltic States, the Balkans, Crete, Spain, Portugal, Italy, and—although very rarely—in the Maritime Alps. In 1939, an inquiry indicated that there were fewer than 50 cases in Great Britain and that none were indigenous.

Epidemiology.—The disease is not highly communicable—a fact which may seem surprising in view of the elaborate measures that were once taken to avoid all contact with patients who had leprosy. Cochrane agrees with the early contention of Rogers and Muir that close and prolonged contact with leprosy during childhood is a very important cause of infections, there is now conclusive evidence against the earlier belief in hereditary transmission. In one study of 700 cases, it was found that about 80 per cent of those infected had lived in the same house as a leper and that 30 per cent had actually shared the same bed. As evidence of the importance of prolonged as well as close contact, and to set these igures in perspective, it should be noted that only 3–5 per cent of those ho live in the same house as a leper actually acquire the disease.

The incubation period seems to be between two and three years and e disease is very liable to appear about the age of 12 to 14 years; about f of all who are infected show the disease before the age of 20 years, l about three-quarters show it before they are 30 years of age. Males affected twice as often as females.

The actual route of infection is still under discussion. It was long held that the organisms gained entry through the nasal mucosa, but Rogers

maintains that they pass directly through lesions in the skin, often minor abrasions or perhaps insect bites.

Types of Leprosy.—As already mentioned, the skin and nerves are the tissues mainly, though not exclusively, involved. Mixed types are common, and the bacilli may produce other lesions, notably in the mucous membrane of the nose. The 1938 Cairo Congress adopted the following classification :—

1. Lepromatous (Cutaneous) type.—L1, L2, and L3, indicate early, moderately advanced, and very advanced cases respectively.
2. Neural type.—N1, N2, and N3 represent degrees of progress

Sub-divisions of neural type.—Anæsthetic (Na) (polyneuritic), Simple Macular (Ns) (with flat macules); Tuberculoid Macular (Nt) (minor and major).

Mixed cases are indicated by combining the symbols L and N with the figures indicating the stage and with the letters indicating the subdivisions of the neural type.

Clinical picture

[illegible] form of [illegible] adı [illegible] 1928 and 1944 . mixed type 49 9 per cent., lepromatous 39·1 per cent., and neural 11 0 per cent. (In recent years 31 cases were labelled tuberculoid.) Anæsthesia and the characteristic skin lesions (leproma nodules) are thus the two most important clinical features of leprosy, but there are many others. Anæsthesia is perhaps the most significant because it may be the first and only symptom for months or years. The common clinical features will now be briefly described in turn.

Anæsthesia.—Testing for *anæsthesia is not always easy in patients* suspected of leprosy. A useful routine is this: Touch several normal [illegible] With his eyes open the patient [illegible] sense last.

Anæsthesia is most often detected on the ulnar aspects of hand and forearm, the outer aspects of leg and foot, the buttocks, and the pinna of the ear.

Macule formation.—Along with the anæsthesia, macules commonly appear in the skin giving rise to the classical maculo-anæsthetic form of neural leprosy. The appearance of macules may be accompanied by fever and lassitude, but this reaction is not constant. Urticarial rashes sometimes appear.

At first the macular patches are completely flat or only a little raised and their borders are sharp, later, as the macules enlarge and grow either paler or redder than normal skin, their borders become elevated. In these elevations, a few bacilli may be found, though they are absent from the central, now anæsthetic, part of the macule itself.

The macular area loses the power to sweat even after pilocarpine administration; it becomes smooth and scaly, and hairs break off.

Nerve trunk Involvement.—Scanty bacilli first invade the terminal nerve fibres and sheaths of nerves, which become infiltrated with mononuclear cells, and show degenerative and fibrotic changes. The process spreads up the nerve trunks but does not reach to the spinal cord. Spindle-shaped enlargements or beadings appear along the course of the nerves, the beads are at first tender but later become insensitive. They should be searched for on the ulnar nerve behind the elbow, the external peroneal at the upper end of the fibula, the great auriculars in the neck, the radials, the supra-orbitals, and others. The ulnar is the commonest site.

Several important consequence follow upon the nerve lesions: there is anæsthesia and muscular weakness, fingers or toes are often lost because the anæsthesia favours accidents, trophic changes develop in the skin, with consequent blisters and ulcers, and in bones, with osteoporosis and weakening. These bone changes, combined with muscular contractures, lead to the severe and terrifying deformities—claw-hand, for example—which gave leprosy its special place in ancient communities.

Lepromatous nodules.—These nodules, or lepromata, which develop in the skin, are the most characteristic lesions of leprosy. They tend to appear in crops, and their appearance is often associated with attacks of irregular fever during which leprosy bacilli may enter the blood stream in sufficient numbers to be demonstrable in the centrifuged deposit of 5 to 10 c.cm. of citrated blood.

The nodules are reddish-brown in colour and may be very small or over 1 inch in diameter. They contain masses of bacilli either free or within cells, they indicate a more severe and more contagious type of the disease than neural leprosy, and they often ulcerate. In the lepromatous form of leprosy, the skin of the face becomes thickened, the eyebrows are lost, and lesions in the nasal mucosa are common. These often lead to collapse of the nasal septum, and this completes the picture of the characteristic leonine facies.

Other lesions.—Corneal ulceration, iridocyclitis, and lesions of the mouth and larynx, are all more common in lepromatous leprosy than in other forms. The lymph glands and internal organs are sometimes affected, especially the liver, testicles, and ovaries.

Tuberculoid macular leprosy.—This form deserves a special note because it is important that it should be distinguished from lepromatous leprosy. The dermal tuberculoid lesions are localized, often associated with nerve beadings, and contain very few bacilli. They indicate a high degree of resistance and respond well to treatment. The major forms contain more bacilli than the minor forms, and they have margins that are more clearly defined, therefore, they are easier to recognize.

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of leprosy may not yet have become anæsthetic, and bacilli may
demonstrable in scrapings from the nasal mucosa or from a
of excised skin, and the characteristic histological changes may
recognizable. Suspected patches should always be carefully
d for the presence of ringworm fungi.
rosy the macules are most common on the lobes of the ears, alæ
ose, forehead, eyebrows, cheeks, and chin. They also appear on
ensor surfaces of the forearms and thighs and on the buttocks.
lms of the hands, soles of the feet, and hairy portions of the scalp,
, and axillæ are rarely affected.
re is often diffuse thickening of the skin of the forehead above the
ows associated with a *peau d'orange* appearance, which is very
stive to those familiar with the picture. At a later stage the skin
nes furrowed, nerve beadings may appear in the usual situations
Clinical Picture above), and lepromatous nodules may begin to
lop By then the disease is relatively advanced and its recognition
sy for those familiar with leprosy. Trophic changes, perforating
rs, and the characteristic advanced deformities like leonine facies
claw-hand present a picture that few will mistake for anything else.
lepromatous cases, bacilli are easily found in material scraped from
incised nodule or even from natural exudation on the skin surface
r the affected area. In neural leprosy, bacilli are often very scanty
d may not be found. A small clip of skin taken from the lobe of an
parently normal ear will sometimes show bacilli if its under surface is
bbed on a slide which is then stained.
Scrapings from the nasal mucosa, nasal discharge, or a nasal swab will
positive in advanced cases but a negative result is not of value. During
ever, bacilli may appear in the blood (*see* Clinical Picture above)

Demonstration of bacilli.—Films are stained by a modified Ziehl-Neelsen method* and the organisms are easily recognized by their acid-

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* Modified Ziehl-Neelsen method for *B lepræ*.

(1) Make a film, dry and fix it by heat in the usual way

(2) Flood the slide with filtered, strong carbol-fuchsin which has been gently heated in a test tube to the point where steam begins to rise
Allow to act for five minutes, applying enough *gentle* heat (from a spirit flame) intermittently to keep the preparation steaming. The stain must not be allowed to dry on the slide

(3) Wash with water.

(4) Immerse the slide in 5 per cent sulphuric acid (20 per cent is used for tubercle bacilli) After about one minute, remove the slide, wash it in water, and replace it in the acid. Repeat several times till the slide is a faint pink colour. Wash in water

(5) Counterstain with methylene blue for one to two minutes

(6) Wash, dry in air with the aid of gentle heat but without blotting, examine under oil

fastness, their slender beaded form, and their aggregation in masses either inside monocytes (lepra cells) or free in the tissue or exudate.

Differential Diagnosis.—The following may be confused with leprosy:—

(1) *Syphilis.*—The Wassermann and Kahn tests may be misleading since they are sometimes positive in leprosy uncomplicated by syphilis.

(2) *Leucoderma.*—Here the white patches are not anæsthetic and they are usually much more extensive and symmetrical than those of leprosy.

(3) *Syringomyelia.*—Here the nerves are not thickened, although the anæsthesia is like that of leprosy.

(4) *Tinea.*—Demonstration of the causal fungus is easy.

(5) *Leishmaniasis.*—The muco-cutaneous form affecting the nose and mouth and the post-kala-azar dermal form may cause difficulty. Seek for leishman-donovan bodies.

(6) *Psoriasis.*—There is no anæsthesia and leprosy bacilli are not found.

(7) *Lupus erythematosus, tuberculosis,* and *yaws* may all resemble leprosy in some particulars and cause difficulty to those not familiar with the characteristic features of each.

Prognosis.—At the beginning of treatment the prognosis should alway be guarded, much depends on the type of case. Thus Hopkins and Fagei from the National Leprosarium, U.S.A., have shown that the duration of cases of all types combined, from admission to death, averaged only 10.3 years. In neural cases average duration was 14.5 years, in mixed 10.6 years, and in lepromatous cases 9.3 years. On the other hand only one tuberculoid case was fatal, 18 years after onset. Of 723 patients, 145 were discharged with disease arrested and only 16 relapsed. Out of total of 190 deaths, 55 were the result of nephritis and 37 of tuberculosis; nly 26 were the direct result of leprosy itself—most often ashpyxia from leprous laryngitis.

Some very early nerve cases appear to recover spontaneously without treatment. At the opposite extreme, acute febrile cases may die in two to three years.

Lepromin test.—This is roughly analogous to the tuberculin test and its significance is prognostic rather than diagnostic. It is carried out by the intradermal inoculation of sterilized lepromatous material—that is, material containing many dead bacilli. Recently, various fractions have been used in place of the crude material. A positive result is shown by a red zone in 24 hours and a late reaction in seven to ten days in the form of induration which may persist for some time.

A negative reaction in a case of proved leprosy is an unfavourable sign, a positive reaction indicates good powers of resistance.

Treatment.—Many ineffective drugs and procedures have been employed in the treatment of leprosy. Proper diet and good hygienic surroundings are probably just as important as drug therapy even with the most modern preparations of chaulmoogra and hydnocarpus oils. A few doses of tartar emetic intravenously or fouadin intramuscularly (see

Schistosomiasis) have been used for the treatment of general reactions when that is necessary.

In any event, the details of treatment are matters for those already experienced in management of the disease. The International Leprosy Congress (1938) advised the administration of chaulmoogra oil or its ethyl esters *intramuscularly, subcutaneously, or intracutaneously.* They should not be used during leprous fever or for cases complicated by tuberculosis or nephritis, and they should not be given intravenously. *By mouth they often upset* the stomach.

The following doses have been suggested :—

Chaulmoogra oil.—3 *per cent. solution injected intramuscularly or sub*cutaneously, 0·5 c.cm. increasing to 5·0 c.cm. for each dose given twice weekly.

Ethyl ester preparations.—1·0 to 5·0 c.cm. intramuscularly or subcutaneously in increasing doses twice a week.

Smaller doses may be given intracutaneously to infiltrate the lesions.

These drugs help in retarding the disease; but, as already indicated, the essence of treatment is wise management of nutrition and of complicating disabilities—for example, ancylostomiasis or other infestations—com- [illegible] available for [illegible]

Prophylaxis.—The essential measure of prophylaxis is segregation of as many as possible of those with leprosy in the active, infectious state. Perhaps the most important phrase is "as many as possible", for the [illegible]

cealed. Success has attended the plan of allowing early cases of little or no infectivity to be treated as out-patients of hospitals or special *dispensaries. In some parts of tropical Africa,* agricultural colonies with model villages associated with out-patient dispensaries *have* been established and have proved both practicable and valuable.

Other measures are routine examination of school children and periodic examination of known contacts in order to detect and treat new cases *in their early stages.*

LEPTOSPIROSIS ICTEROHÆMORRHAGICA

This form of infectious jaundice is often called Weil's Disease.

Etiology.—*Leptospira icterohæmorrhagiæ* the causative organism is found in the blood, urine, cerebro-spinal *fluid* and *bloody sputum.* Leptospira is a form of spirochæte in which the spirals are in close apposi- [illegible]

Some authorities consider there is no valid reason to subdivide the group Spirochætacea into many genera and subgenera, such as Spironema, Treponema, Leptospira, etc. Accordingly, they recognize only two genera:—

(a) *Spirochæta* (including Leptospira). These are actively motile, have a non-rigid flexible body with tapering ends; and do not possess terminal flagella.

(b) *Spirillum.*—Actively motile with a rigid, inflexible, spiral body with tapering ends; possess one or more terminal flagella at each end.

According to this nomenclature there are three species of the genus *Spirochæta* pathogenic to man —*Spirochæta recurrentis*, the cause of both louse- and tick-borne relapsing fever, *Spirochæta pallida*, the cause of syphilis and of that closely-allied disease, yaws, and *Spirochæta icterohæmorrhagiæ*, the cause of Weil's disease. Of the genus *Spirillum* there is only one species pathogenic to man, *Spirillum minus*, which causes one form of rat-bite fever.

Rats and other small rodents serve as hosts *Rattus norvegicus*, *R alexandrinus*, *R rattus*, the mouse, *Mus musculus*, and the Japanese vol *Microtus montebelloi*, may all pass leptospiræ in their urine and fæces. The bandicoot, the dog, and the fox have also been said to be carriers, the dog appears to act as a reservoir of infection in some districts (Antwerp, California)

Canine infections with *L. icterohæmorrhagiæ* are to be differentiated from those due to *L. canicola*, which has been described in infectious jaundice in dogs, but has been identified only rarely in the human subject, mostly in cases without jaundice It is believed that the disease was originally an epizootic in rats, but that these rodents have become immune and now act merely as reservoirs of infection The portals of entry to the human body are not exactly known, but it is believed that infection takes place both through the naso-pharynx and through skin abrasions, possibly by means of infected food or water. Organisms indistinguishable from this Leptospira have been isolated from pools of dirty water in mines and elsewhere.

Spirochætal jaundice is specially prevalent in Japan, where the causative Leptospira was first isolated from rats by two Japanese workers, Inada and Ido (1914) The disease was also prevalent during the 1914–18 war, especially on the Western Front. Recently, outbreaks have occurred in this country among certain occupational groups in close contact with rats, such as London sewer workers, Aberdeen fish cleaners, etc. In consequence, spirochætal jaundice is now officially classed as an occupational disease and comes under the provisions of the Workmen's Compensation Act.

In 1936 a number of cases occurred among soldiers in the Aldershot district, most of whom had bathed in the Basingstoke Canal. Twenty-five per cent of the rats inhabiting the banks of this canal were found to harbour *Leptospira icterohæmorrhagiæ* Cases have also occurred among troops in Northern Ireland, Italy, and Normandy.

Weil's disease is rare in the Middle East, only a few imported cases, all among naval ratings, having been reported in the Middle East Force during the 1939–45 war From June to December, 1944, a total of

39 cases were notified in the British Liberation Army; the majority of infections were acquired in Normandy.

Recent reports show that the disease is widespread; the Dutch East Indies, Borneo, Cochin China, Indo-China, the Andaman Islands, Malay States, India, China, and Australia all reporting cases that have been proved bacteriologically. Since 1937, when Das Gupta and Chapru reported the first bacteriologically-proved case in India, many cases have been diagnosed in that country.

Many cases have been notified in wet mines, especially in Japan and Scotland; the disease has also been prevalent among sugar workers in Queensland following prolonged rain and in flooded rice fields in China and Senegal.

Slime fever, mud fever, swamp fever, and marsh fever are other labels for leptospirosis in South East Europe. Spirochætes serologically different from *L. icterohæmorrhagiæ* have been isolated from some of these cases—usually from milder, non-icteric infections.

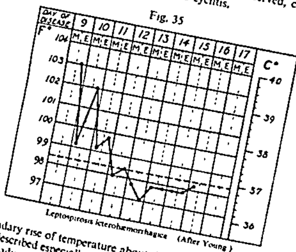
In Europe leptospirosis occurs chiefly in the late summer and autumn, in Japan, September to November are the months of greatest prevalence.

Symptoms.—The general course of the disease is as follows: After an incubation period of six to 12 or more days, the onset is acute with rigors, vomiting, headache, and pains in the neck, back, and limbs. Muscular tenderness is often acute, especially in the lower limbs. Patients complain of unsteadiness and inability to stand. There is usually irregular fever, the temperature varying between 103° and 105° F. and falling by lysis often from the fifth to the tenth day (Figs. 35 and 36) Following a period of low pyrexia or of normal or subnormal temperature there is often a secondary rise towards the end of the second week which may continue as long as a further week before the temperature finally settles. Intense lassitude and severe prostration are common. Jaundice shows itself about the fourth or fifth day of the illness and deepens until the ninth or tenth day, when it fades rapidly. The conjunctivæ are injected and jaundiced. This conjunctivitis (pink eye) occurs in a high percentage of cases and is of considerable diagnostic importance. The colour of the skin is lemon or orange, rarely greenish. Sometimes it has a peculiar hue owing to a combination of yellow jaundice and red vasomotor dilatation of surface capillaries Pruritus is rare. It is important to note that jaundice may be absent. Rashes—erythematous, measly, and petechial—have been described. The urine is high coloured and nearly always contains albumin, sometimes in large amount and with numerous renal casts; bile is usually present in jaundiced cases and there is also a large excess of urobilin; the urine also frequently contains red blood cells and may be obviously blood-tinged. *Leptospiræ may* be present in it, but are difficult to demonstrate. The tongue becomes very dry, brown, and fissured. Labial herpes is common and the bullæ may be hæmorrhagic.

The pulse is slow in the later stages and the blood pressure low. There is generally a leucocytosis of 10–12,000 or more per c.mm. and a differential count in the acute stage shows an increase of polymorphs. Later a lymphocytosis is found. The fæces are pale and there is usually a good deal of gastro-intestinal disturbance. Constipation is the rule.

The liver may be enlarged, splenomegaly is less common. Sometimes the hepatomegaly is sudden and so marked that it gives rise to pressure dyspnœa. The gall bladder is distended and tender on palpation. The superficial lymphatic glands, especially those in the groins and axillæ, are frequently palpable. Other points worthy of note are that in bad cases typhoidal, uræmic, and meningeal symptoms may occur. Leptospiræ may be found in the cerebro-spinal fluid of a proportion of those with meningitis. Hæmorrhagic cases are not common, but are usually dangerous Epistaxis, hæmaturia, melæna and bloody sputum have been noted Various ocular changes have been observed, chiefly of an inflammatory nature like iritis and irido-cyclitis.

Fig. 35



Leptospirosis icterohæmorrhagica (After Young)

A secondary rise of temperature about the beginning of the third week has been described especially in the older accounts of Weil's Disease

The malady appears to be more severe and more often fatal in hot countries. It leaves behind it a varying degree of anæmia and considerable debility, often rendering the patient ineffective from a military standpoint for four or five months. In some cases a renal sclerosis has been noted.

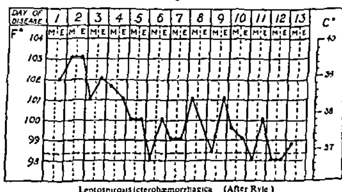
The disease may vary in intensity from the severe toxic form, just described, to a mild febrile disturbance in which the temperature may never reach 100° F The intermediate grades of severity may show a few days' fever, continuous or intermittent, with or without relapses, and sometimes there is a close resemblance to dengue In all, however, injected conjunctivæ and a trace of albumin in the urine appear to be constant signs There are different serological types of *Leptospira* although there are cross-reactions between some of these. Among these may be mentioned *L. icterohæmorrhagiæ*, the cause of classical Weil's disease, *L. canicola*, the cause of canine jaundice, which rarely infects man, and *L. grippotyphosa* the cause of the swamp fever (mud ever) of Eastern Europe It is said that jaundice has never been noted

in swamp fever or in human infections with *L. canicola*. In Japan further types have been recognized—for example, *L. hebdomadis*, which causes seven-day fever, another mild form of Weil's disease, and *L. autumnalis* which causes a more virulent form clinically closely resembling classical Weil's disease. Other strains recognized are: *L. sejroe*, *L. bataviæ*, *L. pomona*, *L. australis A*, and *L. australis B*.

The mortality is variable, ranging from 4 to 32 per cent. in European outbreaks to as high as 48 per cent. in Japan.

Diagnosis.—The Leptospiræ are present in the blood during the first few days of the febrile period, but are usually few in number, and it is generally necessary to inoculate a guinea-pig to demonstrate their presence. Direct examination of the blood by dark-ground illumination is not

Fig. 36.



Leptospirosis icterohæmorrhagica (After Ryle)

advised, it has led to many false-positive reports through the inexperienced being misled by artefacts. The guinea-pig should be inoculated intraperitoneally or by rubbing the blood or (after the first week) urine on the shaved or lightly scarified skin of the abdomen. With the urine this should be done at the patient's bedside as the Leptospiræ rapidly disintegrate in urine that is allowed to stand even for short periods, especially if acid. After the death of the animal, which usually occurs in 10 to 12 days, they may be seen in large numbers in the liver. After the first week of the disease the Leptospiræ should be searched for in a centrifugalized specimen of urine. Inada has found that most cases pass spirochætes in the urine after the twentieth day.

The agglutination test for immune bodies is essentially simple but it requires skill and experience, therefore it is usually carried out in reference laboratories. The titre rises during the first two or three weeks of illness. Two samples should be sent for examination.

Differential Diagnosis.—Distinguish from infective hepatitis.

Yellow fever, cerebro-spinal fever, relapsing fever, plague, rat-bite fever, dengue, malaria, especially the so-called "bilious remittent fever", and several other acute diseases may simulate leptospirosis icterohæmorrhagica. It should be remembered that *in Weil's disease there is almost*

invariably some evidence of the hæmorrhagic tendency which may take the form of hæmoptysis, epistaxis, petechiæ into the skin, hæmaturia melæna, or subconjunctival hæmorrhage. Noguchi confused Weil's disease with yellow fever when he described his *Spirochæta icteroides* (identical with *L. icterohæmorrhagiæ* and *S. interrogans*) as the cause of yellow fever

Prophylaxis.—Disinfect urine, fæces, and bloody sputum Urine may contain Leptospiræ for several months, generally in small numbers after the fortieth day.

Destroy rats and prevent their access to food or premises (see Plague) Prevent insanitary conditions generally, and pay particular attention to water supplies. Protective inoculation with a vaccine prepared from killed cultures of *L. icterohæmorrhagiæ* should be considered in the case of those at special risk (*i.e.* laboratory workers, London sewer workers, etc.). Rat-infested water should be avoided for bathing, washing, or drinking.

Importance is not to be attached to the mere finding of leptospiræ in water which is under suspicion because it is very common to find there organisms like *L. biflexa* and other non-pathogenic spirochætes which require close cultural study for their identification Laboratory infections with leptospiræ are by no means uncommon and rubber gloves and masks should be worn by those handling infected rats or discharges.

Treatment.—The specific serum if available should be given without delay in doses of 20–60 c cm intravenously, and repeated for several days Otherwise the treatment is chiefly symptomatic. Flush the patient freely and, if necessary, cup over the kidneys The condition of the liver would indicate the administration of glucose, at least in bad cases Ten per cent. solutions may be employed intravenously The serum of convalescents by the intramuscular route in daily doses of 30 to 40 c cm has been recommended Penicillin is under trial and promises well according to some reports. Large doses must be given early in the disease if any benefit is to be gained.

LYMPHOPATHIA VENEREUM

Lymphopathia venereum.—Synonyms for climatic bubo, lymphogranuloma inguinale, fourth venereal disease.

This is a widespread contagious disease, usually acquired by sexual intercourse, due to an ultramicroscopic filterable virus, communicable to most laboratory animals The initial lesion consists of a small often transitory herpetiform lesion on the genitalia or perianal region This is followed by an inflammatory reaction in the regional lymphatic glands and surrounding connective tissue (climatic bubo in males) If untreated this usually progresses to suppuration with constitutional symptoms, lassitude, loss of weight, pains in the body, sweating and fever. The disease may affect any age or sex but is more common in the age of greatest sexual desire It occurs in all races and has a world-wide distribution, but is not very common in England

Clinical Picture.—The primary lesion is usually on the genitalia. In males the commonest site is the coronal sulcus; in females it may occur on any part of the external genitals. In both sexes the lesion may be near the anus. The characteristic lesion on the genitals consists of a small herpetiform vesicle or ulcer, sometimes multiple, with clean-cut edges, surrounded by a reddened zone, but not indurated and free from pain or itching. The primary lesion is often small and may escape notice, healing spontaneously. The incubation period is usually less than a week. From this site infection spreads by the lymphatics, which may become inflamed, to the lymph glands into which they drain. In the male, with a primary lesion on the penis, the inguinal glands become involved, in the female or male with an anal primary lesion the perirectal glands are affected. This glandular swelling occurs within ten to thirty days of contracting the infection. The first local symptom is stiffness and aching in the groin followed by swelling. In the early stages the enlarged gland is discrete and movable but tender. The inflammatory process usually progresses to involve all the inguinal group of glands on one or both sides with considerable periadenitis causing fixation of the mass with involvement of the skin. The mass may be as large as a hen's egg. The adherent skin usually assumes a purplish colour. Spread to the iliac glands causing considerable swelling of this group not infrequently occurs. Untreated, spontaneous resolution may occur, but more frequently the gland mass breaks down at several points with the formation of multiple minute abscesses, which eventually open on the surface at one or numerous points. These fistulæ show no induration and exude scanty viscid opalescent pus free from organisms. The process may progress; untreated, it continues for months leading to blockage of lymphatics and consequent swelling of the parts drained by these vessels.

The constitutional symptoms vary, but fever, sweating, headache, loss of weight and nausea are commonly present and may persist for a considerable time. Spontaneous improvement however usually occurs after a variable period. There is no characteristic blood change.

Rectal changes leading to stricture more frequently occur in females. The narrowing is usually situated within 3 to 8 cm. above the anus.

Diagnosis.—The clinical picture is usually sufficient to enable a diagnosi[s] to be made, but this should be confirmed by Frei's test. This is carrie[d] out by injecting intradermally 0 1 c cm of the antigen, which is a sal[ine] extract of affected glands, and as a control a similar amount of norm[al] saline on the other side. The result should be read after forty-ei[ght] hours. A positive result consists of an infiltrated inflammatory do[me-] shaped area, 0 5 cm. or more in diameter, which can be felt as we[ll as] seen.

There may be a small central area of necrosis and a red zone roun[d the] lesion. This test is specific and very reliable.

Differential Diagnosis.—This must be made from other cau[ses of] adenitis, such as sepsis, chancroid, syphilis, tuberculosis, carc[inoma,] Hodgkin's disease, and plague.

Treatment.—The disease often responds well to the sulpho[namides] given in the usual doses. The temperature and general symptom[s]

subside in a few days The adenitis may take a considerable time to clear after all other manifestations of the disease have disappeared. If suppuration has occurred local treatment should be on the usual surgical lines Excision, however, is usually contra-indicated.

MALARIA

Malaria is distributed in the area between 63 N (Russia and Southern Sweden) and 23 S (South Queensland) wherever there is a sufficiency of mosquitoes hospitable to the causative *Plasmodium* together with conditions of temperature and humidity which permit the complete development of the parasite in the infected mosquitoes In these Memoranda it is quite impossible to deal in anything like an exhaustive manner with what is one of the most common and important of human diseases, but an attempt is made to present a concise account of malaria, special attention being paid to prevention and treatment

The Mosquito.—Species of *Anopheles* which allow development of the malaria parasite and which habitually seek buildings and shelters may become dangerous vectors

The following is a list of the more important anopheline vectors of malaria, those with an asterisk (*) can be notorious carriers wherever found —

EUROPE —*Anopheles maculipennis* var *atroparvus** and var *labranchiæ,* *A. sacharovi,* A superpictus**

NORTH AFRICA AND MIDDLE EAST —*A claviger, A gambiæ,* A maculipennis* var *labranchiæ,* A. melas** (*A gambiæ* var *melas**), *A pharænsis, A sacharovi,* A sergenti,* A superpictus**

TROPICAL AND SOUTH AFRICA —*A funestus,* A gambiæ,* A hancocki, A hargreavesi, A melas,* A moucheti, A nili, A pharænsis, A. pretoriensis*

PERSIA AND IRAQ —*A culicifacies,* A sacharovi,* A stephensi,* A. superpictus**

INDIA AND CEYLON —*A. annularis, A culicifacies,* A fluviatilis,* A jeyporiensis, A minimus,* A. philippinensis, A stephensi,* A sundaicus,* A superpictus,* A varuna**

FAR EAST —*A aconitus, A barbirostris, A culicifacies* A hyrcanus sinensis A jeyporiensis candidiensis, A kochi, A leucosphyrus A maculatus,* A minimus,* A pattoni,* A subpictus, A sundaicus,* A umbrosus*

AUSTRALIA AND NEW GUINEA —*A annulipes A bancrofti, A punctulatus**

NORTH AMERICA —*A quadrimaculatus**

CENTRAL AND SOUTH AMERICA AND WEST INDIES —*A albimanus,* A darlingi**

It must be understood that a species of *Anopheles* capable of carrying malaria may have little or no epidemic importance by reason of its

habits. But it must be understood, too, that the habits of even the same species may not be the same throughout the whole of its range. In Palestine, for example. *A. claviger* haunts houses and is a *most important carrier*, whereas in Northern Europe it is an outdoor mosquito.

It has been recognized in recent years that within certain species of anopheline mosquito there exist varieties, whose individual characteristics are indistinguishable except in certain minute respects; yet the varieties differ markedly in their habits and capabilities of transmitting malaria.

For example · *A. maculipennis*, an important vector of malaria, exists and breeds freely in many parts of this country, where indigenous malaria is rare, and also in Holland, where it is common, especially in the Northern districts.

Formerly, it was difficult to explain this discrepancy in the incidence of malaria in two countries in both of which there flourished an apparently potent malarial-transmitting species of anopheline mosquito. But this *apparent anomaly can now be explained in terms of the different varieties* within the one species of *A. maculipennis* found in the two countries.

In the Northern districts of Holland where malaria is endemic the

On the other hand the variety commonest nowadays in England is *A. maculipennis messeæ*, which, largely on account of its habits, is a poor vector of malaria. This variety shuns human habitations, breeds only in

ranchiæ,

till con-*sidered by some authorities not to be a separate species but a variety of A. maculipennis*

It must be emphasized that the anatomical differences between the above varieties are minute, and the differentiation is usually made by the characteristics of their eggs (surface pattern and air floats)

Medical officers serving in the tropics will find it of interest and value to make themselves familiar with the local anophelines and their respective breeding-habits and seasonal variations, and to try to ascertain the degree of responsibility of each in spreading malaria.

The Parasite.—The four recognized species of malarial parasite pathogenic to man are *Plasmodium malariæ*, *P. vivax*, *P. falciparum*, and *P. ovale*. A fifth, *P. tenue*, said to be common in the North East and Central India, has not received general recognition. *P vivax* and *P. ovale* produce a clinically similar so-called benign tertian fever, *P. falciparum* produces a malignant or subtertian fever; whilst *P. malariæ* produces a quartan fever

The sexual forms (gametocytes) of quartan and benign tertian, *i e, those* adapted for life and development in the mosquito, are spherical, while the gametocytes of malignant tertian are crescentic or sausage-shaped (Plate 21).

On reaching the mosquito's stomach the male parasite (micro-

gametocyte) develops flagella (microgametes) which play the part of spermatozoa. These enter and fertilize the female parasite (macrogamete) which is formed from the female gametocyte (macrogametocyte) as the result of certain nuclear changes. The body resulting from this union is known as the zygote, which now becomes motile (ookinete or travelling vermicule) and, penetrating the stomach wall of the mosquito becomes encysted under its outer limiting membrane to form the oocyst. In heavy infections the outer aspect of the stomach may be studded with oocysts. The contents of these cysts divide to form vast numbers of spicular rod-like bodies, the sporozoites. The oocyst, which has increased greatly in size, finally bursts, and the contained sporozoites are thrown into the hæmocele (the "blood bath" surrounding the intestinal canal of all arthropods, which takes the place of the blood vascular system of vertebrates) and thence find their way to the salivary glands of the mosquito, which is now infective.

The whole process may take about twelve days to accomplish, but the period varies according to climatic and other conditions, and the mosquito may remain infective for many months. When she feeds and injects saliva the sporozoites are carried down the salivary canal in the hypopharynx and into the skin. The immediate fate of the sporozoites is not known. It is doubtful if they penetrate directly into red blood cells. Some hold the view that, as in bird malaria, they first develop in cells of another type (possibly of the reticulo-endothelial system). This hypothetical phase is known as the *extra-* or *exo-erythrocytic cycle*. Eventually young parasites appear in the red cells, they increase in size, produce and retain, scattered throughout their protoplasm, the *malarial* pigment, hæmozoin (melanin), and destroy the containing red cells. There is now no question of male and female forms, for multiplication within the human host is *non-sexual*. Each young parasite within its *host* cell grows larger and larger until the time has come for it to divide. By this time the parasite, if belonging to the species *Plasmodium vivax* (benign tertian) is so large that it has greatly distended the red cell containing it, which moreover, has become stippled (Schüffner's dots). These Schüffner's dots which appear in the parasitized red cell and *not* in the infecting plasmodium, are due to an alteration in the staining reaction of the former due to the presence of the growing parasite (trophozoite) within it and are not excretory products (such as, for instance, hæmozoin) elaborated by the latter. They appear in a proportion of red cells parasitized by all stages of *Plasmodium vivax* beyond the young ring stage (*i.e.* trophozoite, schizont, gametocyte) (Plate 21, *a*).

With quartan and malignant tertian parasites (*P. malariae* and *P. falciparum*) this enlargement of the host cell does not take place nor do Schüffner's dots appear, although in the case of malignant tertian certain dots (Maurer's dots) may appear within the red cell; these are by no means constant and are best seen in well-stained slides (Plate 21, *c*). In the case of *P. ovale* the red cell becomes stippled (often heavily) with Schüffner's dots and may be oval in shape (hence the name) and the edges may be frayed (Plate 21, *d*). In all cases, however, division takes place, the one original parasite (schizont) dividing into many merozoites,

the number varying with the species. quartan and ovale, eight to twelve, benign tertian, fifteen to twenty-six; malignant tertian, eight to thirty-two These clumps of merozoites constitute the mature *schizont and correspond to a full* ripening of the parasite. The membrane of the damaged red cell then gives way and the merozoites are poured into the blood-stream. Some are engulfed by phagocytic white cells, others enter fresh red blood corpuscles and start again the *non-sexual cycle. This process of intra*corpuscular development, *i.e.* from entry to burst (known as schizogony in contrast to the sexual cycle within the mosquito known as sporogony), naturally takes some time, and the time varies with the species of parasite In quartan infections it takes seventy-two hours, and in the tertian infections (including ovale) it takes forty-eight hours

The origin of the different names is now apparent, for stages in the life *cycle of the parasite correspond to stages in the clinical picture of the* malarial attack. The hot stage with the temperature high is when the parasite is young, and just beginning to grow in the red cell; the fever-free

[illegible]

on the third day. The same should be, and sometimes is true of a malignant tertian, but often its pyrexia is quite irregular, being sustained or remittent, while quotidian forms are recognized

These interesting facts are best realized by a study of the diagrams shown in Figs. 37, 38, 39.

[illegible]

mental periodicity of the infecting parasite or to double or triple infections with the same species of parasite. *These greatly alter the characteristic* temperature waves.

[illegible]

infected red cells.

A hiatus has yet to be filled in our description of the parasite. It will be remembered the account began by mentioning sexual forms (gametocytes) in the blood. These are formed from the ordinary parasites of the non-sexual cycle. Certain of these become what is called sexually differentiated. Instead of proceeding in the usual way to schizogony they grow within their host cells either into special spherical (quartan and

[illegible] (malignant tertian) forms Male and female

[illegible]

non-fever-producing forms, and their sole function is to initiate that sexual cycle in the mosquito which has just been briefly described. The gametocytes of all four varieties (especially the crescents of *P. falciparum*) are highly susceptible to pamaquin. Gametocytes of *P. vivax* and *P. malariae* are also susceptible to the action of quinine and mepacrine, but *P. falciparum* gametocytes resist these two drugs. (*See* Table on p. 201.)

Symptoms and Diagnosis

Symptoms.—It may be said at once that at the outset of many malarial attacks, and in the case of most sub-tertian infections throughout the attack, a definite diagnosis cannot be made in the absence of blood examination.

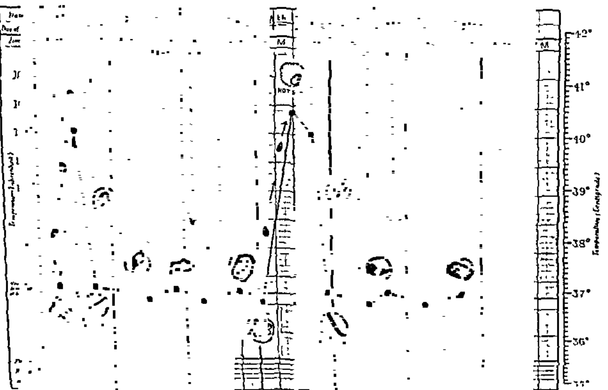
The incubation period varies, but is often about a week or ten days for malignant tertian and somewhat longer in the simple tertian and quartan types, occasionally the patient develops what appears to be his primary attack of malaria months, perhaps, after returning home from the tropics. In many cases, especially of benign tertian fever, the first clinical attack takes place in the early Spring before mosquitoes are prevalent, presumably the result of infection the previous Autumn. These delayed primary attacks are especially common in those who have taken suppressive therapy during the summer malaria season, and above all in those who have relied on suppressive treatment without giving enough attention to measures of personal protection.

In many cases the symptoms of a benign malaria infection commence with an initial stage of continued fever lasting for several days without paroxysms, seemingly due to an irregular sporulation of the parasites, terminating by lysis and often followed by a "silent" phase. Thereafter the disciplined febrile attacks of classical malaria occur. In benign tertian malaria, the earlier paroxysms may have a quotidian periodicity, becoming tertian later.

There may or may not be a premonitory stage wherein the patient feels upset, is tired, has an ache in his bones, perhaps a headache, loses his appetite, possibly vomits and suffers from chilly sensations. At this period his temperature may already have begun to rise, and later on the fever fit fastens upon him. In many cases, however, he finds himself suddenly in the grip of ague, suffering from a definite rigor and such an intense feeling of cold that his teeth chatter and he shivers and shakes.

Very few of the diseases dealt with elsewhere in this series has such a severe and well marked onset as is seen in a typical ague attack. Very often the patient begins to vomit violently. He piles clothes upon himself and yet his temperature is elevated, the sensation of cold being entirely subjective. Then comes the stage of heat and febrile distress, with flushed face, rapid pulse, intense headache, frequent vomiting, quick breathing and dry burning skin, during which the temperature often runs up to 105 F. and the coverings are cast impatiently aside. There may be a slight delirium. Anon the sweating stage supervenes, the perspiration pouring from the patient and soaking everything on and about him. The fever rapidly declines and comfort takes the place of acute misery. The patient though possibly tired can be though he should certainly not

Fig 37.—Disease—Quartan Malaria.



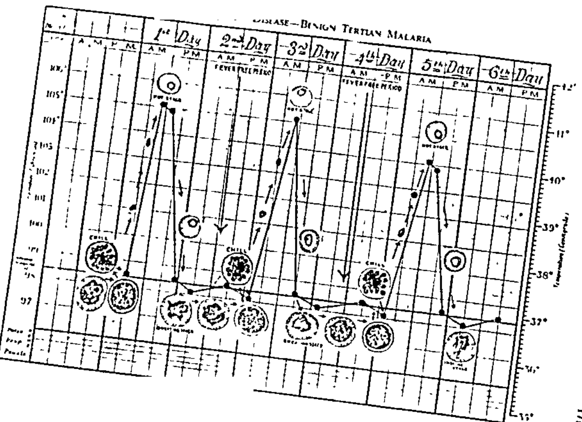
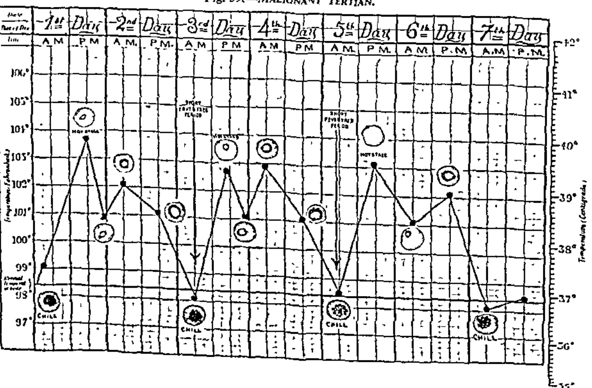

DISEASE—BENIGN TERTIAN MALARIA
1st Day
2nd Day
3rd Day
4th Day
5th Day
6th Day
A.M.
P.M.
FEVER FREE PERIOD
CHILL
HOT STAGE
105°
104°
103
102
101
100
99
97
42°
41°
40°
39°
38°
37°
36°
35°
Temperature (Centigrade)

Fig. 39.—Malignant Tertian.



up and about. Then, according to the nature of the infection, one, two or three days later the fever fit recurs (Fig. 40).

It lasts as a rule from six to ten hours, say one hour for the cold stage, three or four for the hot period, and two to four for that of defervescence. The spleen enlarges during the febrile paroxysm and the urine varies according to the stage and may contain albumin.

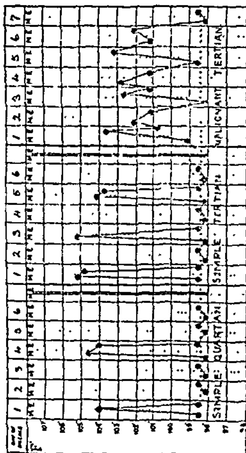


Fig. 40

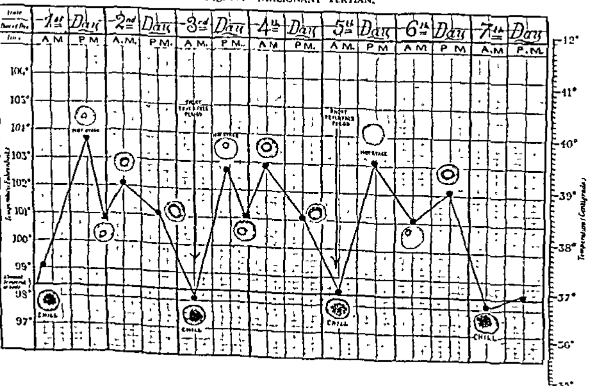
Malaria Charts.

The above is a classical form of intermittent malarial fever. On the other hand, all kinds of abnormal attacks [illegible]

[illegible]

as on the nose or pinna of the ear, is a common symptom, especially in

Fig. 39.—Malignant Tertian.



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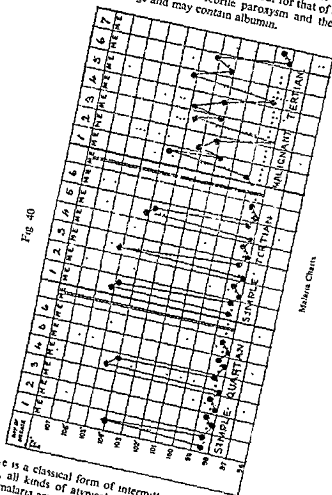


Fig 40

Malaria Charts

The above is a classical form of intermittent malarial fever. On the other hand, all kinds of atypical attacks may occur. Relapses of all varieties of malaria are usually more typical, less severe, and more amenable to treatment than the primary attack.

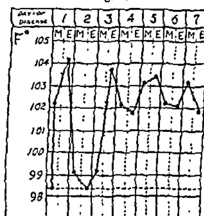
Herpes febrilis, usually round the mouth, occasionally elsewhere, such on the nose or pinna of the ear, is a common symptom, especially in

benign tertian malaria, occurring in about 40 per cent. of cases in Europeans.

Subtertian (*P. falciparum*) infections, more especially primary attacks, are more insidious and dangerous than other forms of malaria. The fever in this variety is prolonged and irregular and does not usually rise to so high a level as in benign tertian or quartan malaria. A temperature over 103° F., especially if it is prolonged at or above this level, must be looked on as serious.

The alternation of hot, cold, and sweating stages is also relatively infrequent or modified in subtertian malaria (Fig. 41) On the other hand, vomiting and severe headache are common; and severe headache is especially important because it may herald a pernicious cerebral attack (Fig. 41). Further, there are clinical varieties of malaria known as bilious and typhoid remittent, the former associated with jaundice,

Fig. 41.



Subtertian malaria showing early tertian fever becoming remittent.

which are very unlike the ordinary attack. During the 1914-18 war such cases were most common in East Africa, but were seen also in Macedonia and Palestine.

The occurrence of cerebral, choleraic, dysenteric, hæmorrhagic, pneumonic and syncopal forms must not be forgotten, and as these very fatal varieties are only too often the result of lack of prompt treatment or are due to faulty treatment, the importance of early and correct diagnosis will be manifest. Moreover, if any case of malaria is neglected it may drift into a state of cachexia, which it is frequently as hard to cure as it is to endure and may lead to a protracted convalescence or permanent invaliding.

As regards coma, it should be noted that it may develop quite suddenly, possibly in a convalescent, especially perhaps when he passes from a hot to a cold climate. It may be preceded by delirium and convulsions or come on without warning Thus it usually resembles either an epileptiform fit or an attack of heatstroke. The patient cannot be roused to

answer questions. He lies and moans. His breathing may be stertorous or quiet. His pupils are often contracted and are like those seen in opium poisoning. His temperature may be high or, and this is important, normal or sub-normal. It is always well to take the rectal temperature in such a case. If not promptly treated he will die. It is important to note that every form of acute cerebral attack may be aped by cerebral malaria. Premonitory symptoms such as very severe headache, photophobia, increased irritability, undue drowsiness, twitchings of the face or extremities, etc., should be watched for. On the other hand, the attack may start abruptly with an epileptiform seizure during the course of an apparently mild malarial attack that has given no special cause for anxiety. Cerebral cases may or may not show a heavy blood infection and a negative blood slide should form no excuse for delaying effective treatment unless malarial infection can be definitely excluded as the cause of the condition. On the other hand, malaria can of course accompany a cerebral catastrophe due to other causes.

The so-called algid type of malaria characterized by collapse, clammy sweat, shallow respiration, subnormal temperature, low blood pressure, vomiting, diarrhoea, and lumbar or epigastric pain, has been shown to be due to an intense infection of the suprarenals.

The term "malignant" is applied to the subtertian variety, which is most common in the tropics, and this form of malaria is the most severe, the most exhausting to the patient, and the most likely to terminate fatally or be followed by grave complications. Benign tertian is always benign but it is important to remember the possibility of mixed B.T. and M.T. infections. Some cases of this class are very severe and cause death with cerebral and other symptoms. Quartan fever, though it induces a very sharp first attack and is very apt to relapse, is not usually serious. For one thing the afebrile periods are longer, for another the number of spores is less.

Spontaneous recovery from malaria can and, in fact, always does occur eventually if the patient lives long enough. If the patient is robust, his phagocytes efficient, the circumstances favourable, and the dose of parasites small, he may vanquish the foe and destroy him altogether. More often he achieves only a partial victory, and the enemy retires, as it were, into his dug-outs in the spleen and liver, and his trenches in the bone-marrow, and awaits his chance of making another raid upon the defences. This withdrawal of parasites is what occurs when, apart from actual cure, a malarial attack comes to an end, or when the disease is controlled, though not cured, by treatment. There seems little doubt that these ordinary non-sexual forms remain there, till a chill or some other factor, such as a surgical operation, causes them suddenly to become active and to start reproducing themselves in the red cells. When the rosettes ripen and the red cells burst, up goes the temperature and we have the phenomena of the relapse.

Within the four recognized species of *Plasmodium* parasitizing man there appear to be many strains which are morphologically alike but immunologically distinct. Strains which are reciprocally protective are called homologous strains, while those for which no such reciprocal

protection exists are called heterologous strains. For instance, the indigenous adult population of an *endemic or hyperendemic focus* of malaria where one strain or homologous strains of, let us say, *P. falciparum* are prevalent may have acquired as a result of repeated infections in their youth complete immunity to that strain or strains. If, however, they are removed to another district where heterologous strains of *P. falciparum* exist, they may suffer from clinical malarial attacks as the result of infection by these new strains against which they have acquired no previous protection. This type of very selective immunity built up as the result of repeated infections with one particular strain or closely allied

[illegible]

case of malaria is of a more general and less highly specific type than premunition, is uncertain and variable in extent.

Complications.—Of the so-called pernicious forms of subtertian malaria by far the most important and dangerous is *cerebral* malaria which is probably caused by mechanical blocking of brain capillaries by vast numbers of parasite-laden red cells, although this simple explanation of the condition has recently been questioned. The possibility of the occurrence of blackwater fever must not be forgotten. Dysentery (*see* p. 98), if actually caused by the malarial plasmodium plugging the intestinal

[illegible]

and other organs in certain cases of malignant infection. A special form of malarial psychosis has been described, but it is doubtful if such exists as a separate entity.

[illegible] modify the course and prejudice the prognosis [illegible] philis, [illegible] minant [illegible] com- [illegible] of malaria [illegible], or traumatic, of a chronically- [illegible] *Special danger attaches, on this* [illegible] of endemic areas, any one of [illegible] ting".

Diagnosis.—If a typical case is seen at the onset of the cold stage, with a history of possible exposure to malarial infection, or indications that the patient may be suffering from a relapse, then the pinched appearance, the chattering teeth, the successive shivers, the enlarged spleen, and the elevation of temperature will, even without blood examination, make a

[illegible] of malaria well-nigh certain. At any rate, if no facilities for

malaria, it is impossible to be sure without a blood examination, and, as regards the use of quinine as a therapeutic test, each case must be judged on its merits, and especially has one to consider the probable nature of the infection (whether benign or malignant) and how long it will take before the patient reaches a place where the diagnosis can be clinched. The principal factors that govern diagnosis are, in order of importance :—

1. The result of examination of one or more well-taken and well-stained thick or thin blood films.
2. History, recent or past, of having been stationed in or having passed through an endemic area of malaria, also a past history of malaria or of febrile attacks likely to have been due to malaria.
3. A careful physical examination, especially of the splenic area. Remember that herpes round the lips is common in B.T. infections in Europeans.
4. Consideration of all the symptoms.
5. Periodicity of the febrile attacks. Quartan periodicity is almost invariable and of great diagnostic value in quartan malaria; tertian periodicity is somewhat less constant in benign tertian malaria, especially in primary attacks, and is usually absent in subtertian infections, especially in the primary attack. Often the first sign of response to malarial therapy is that the completely irregular fever becomes "regimented" to tertian periodicity.

The paramount importance of blood examination was well shown by the valuable results achieved by advanced malaria centres. It must be remembered that a single negative examination does not exclude malaria even when the thick film method is employed, as should always be the case.

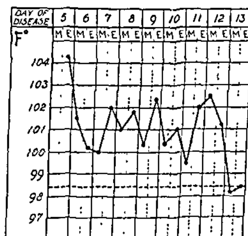
In most localities malaria tends to occur in "rushes", during which the medical and nursing staff are worked off their feet. It is therefore necessary for smooth and efficient working that a satisfactory routine be worked out before the onset of the malaria season. Orderlies and nursing sisters should be instructed in the proper taking of thick and thin blood smears as the medical officer will seldom have time to do this himself.

A close liaison must be established with the attached laboratory, arrangements being made beforehand for the rapid notification by phone or messenger of all positive cases. As part of the routine it is advisable to establish a "priority" list, so that slides from patients for whom, for

any reason, an urgent diagnosis is required, can be examined and reported on before the routine examinations are made. Unless this is done valuable time may be lost in the diagnosis of urgent cases.

Remember also that many slides, perhaps extending over several days, may have to be examined before parasites are found. This is especially the case in primary infections and in those who have taken mepacrine or quinine, either as a therapeutic measure or prophylactically, before admission to hospital. The inhibitory effect of mepacrine on the appearance of malarial parasites in the peripheral blood appears to be considerably less than that of quinine; indeed there is evidence to suggest that a few doses of mepacrine may have a provocative action, parasites appearing for the first time after one or two days' treatment with this drug (*see* Figs. 44A, 44B).

Fig. 42.



Typhoid Fever simulating Malaria. Blood culture positive on 6th Day

Four-hourly films are useful, and it should be realized that the best time to take films is when the temperature is falling. It must also be remembered that the mere finding of malarial parasites in the blood of a febrile patient does not exclude some other cause of that fever. A full physical examination is therefore always necessary, even in microscopically-proved cases.

The vagaries of the disease, the common early stage of continual fever, and the fact that double and even triple infections occur, make malaria difficult to diagnose by clinical examination alone.

Differential Diagnosis.—In this connexion it is instructive to note that in the 1914–18 war cases sent from the Gallipoli Peninsula and definitely diagnosed as malaria by blood examination in Alexandria were provisionally labelled typhoid or paratyphoid. Influenza and rheumatism were other guesses, and there figured also that refuge for the destitute—

pyrexia of unknown origin All manner of diseases have been and may be mistaken for malaria or may accompany that disease.

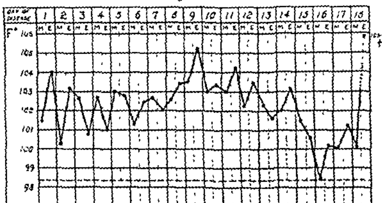
How closely typhoid may resemble malaria and malaria simulate typhoid is shown in a couple of charts (Figs 42 and 43) which explain themselves, and the milder forms may at the beginning be very like paratyphoid. Further, malaria may run concurrently with either of these infections

Malaria may simulate almost any acute or subacute fever and may be called on this account "The Great Mimic" amongst diseases.

Malarial coma may have to be distinguished from heatstroke, cerebral hæmorrhage, uræmia, diabetic coma, and alcoholic and opium poisoning

If malaria parasites have been found in the blood of a patient whose temperature shows no sign of yielding to quinine within three or four days, test the urine for quinine in order to make certain that the drug is

Fig 43.



Malaria simulating Typhoid Fever

being absorbed into the blood Proceed as follows :—First test the urine for albumin If this is absent, add 6 or 7 drops of Tanret's acid solution to 2 c cm of cold, filtered urine in a test tube This should give a dense white precipitate soluble on heating, if quinine is present in ordinary amounts. If the urine contains albumin, add Tanret's solution and boil.

reagent consists of iodide of potash, 3 0 g., corrosive sublimate, 1 0 g., glacial acetic acid, 20 c cm., distilled water to 60 c cm

Treatment

Objects of Treatment.—Sinton has laid down certain criteria for an ideal drug in the treatment of malaria. These are,—

1. It should bring about a rapid cessation of the symptoms complained of and of any acute condition which is likely to endanger life.
2. It should cause no harm to the patient; *i.e.* there should be an ample *margin between the therapeutic and toxic doses to allow of individual* idiosyncrasy.
3. It should destroy all parasites in the body, or at least bring about such a condition that the natural defences of the body can complete the destruction, thus preventing recurrence of symptoms with *reinvasion of parasites into the peripheral blood at a later date.*
4. It should rapidly destroy all the sexual forms of the parasite in the peripheral blood and so prevent the patient becoming a carrier of the disease.
5. It should be effective against all the different species (he might have *added—against the different "strains" also) of the malarial parasite.*
6. It should be cheap (not so important in the case of a military population, an expensive drug, if efficacious, paying for its cost many times over by decreasing hospitalization).

[illegible]

used. Newer synthetic drugs, including paludrine,* have interesting possibilities, but their scope and usefulness remain to be defined by more extended trials than they have yet been given. When the loss of the

[illegible]

at once, intramuscular mepacrine should be administered, the two are

[illegible]

suffering from various degrees of debility and anæmia. They lack the

[illegible]

to sophistication of the quinine before or after issue from the store. Quinine bought locally from bazaar shops or elsewhere should always be suspect on this account. A simple test for the estimation of the quinine content of stock mixtures has been devised.

Then, again, the patient may be unable to absorb the drug in sufficient quantity, a defect sometimes put right by a sharp purge. But if there is any reason, such as the absence of reaction to treatment, to suggest

* Since this edition went to press important evidence has come to hand about the use and action of paludrine. A summarized account appears on p. 353

deficient absorption, the urine should invariably be tested for quinine (p. 179). Quinine may appear in the urine within ten minutes of being swallowed, practically always within two hours, but does not continue longer than forty-eight hours after cessation of treatment.

Quinine.—Quinine is one of several alkaloids, all with some anti-malarial action, extracted from the bark of a shrub, cinchona. It is a quinoline derivative of complex molecular structure and may be administered as the base, quinine, or, more frequently, as one or other of its salts, those most frequently employed being the sulphate, bisulphate, hydrochloride, bihydrochloride, and, for children on account of the absence of the bitter taste common to the other salts, euquinine (quinine and ethyl carbonate).

Action of Quinine.—The malarial parasite may be subjected to selective therapeutic attack at various stages of its life-cycle. There is one phase, the sporozoite (the sporozoite is the parasite in its earliest and pre-infective stage, as injected by the mosquito), which has not yet yielded to anti-malarial therapy.

Drugs which attack the parasite at this stage are known as causal prophylactics or sporozoiticides. No true causal prophylactic, effective in therapeutic doses, has yet been discovered.*

The schizont stage, the clinical evidence of which is the acute malarial attack, yields to many anti-malarial remedies, of which quinine is probably still the most effective. Therefore, quinine is said to be an effective schizonticide

Quinine has definite action on the gametocyte stage of *Plasmodium vivax* and *P. malariæ*, causing benign tertian and quartan malaria respectively, but it has little if any action on the crescents of *P. falciparum* (subtertian malaria). Therefore it is not a universal gametocide; in other words, its sterilizing power as regards the carrier state cannot be relied on.

Relapse Rate.—Exactly what it is that determines relapses in malaria, what happens to the parasites between the relapses, and why some forms of malaria (benign tertian and quartan) are followed by a higher relapse rate than others (subtertian), is not known Quinine and its salts undoubtedly influence the relapse rate of all forms of malaria to some slight extent, but a relapse rate in the neighbourhood of 50-60 per cent. is to be expected if no drug other than quinine is used. This high relapse rate only follows benign tertian and quartan infections. Relapses are less common following subtertian malaria no matter what anti-malarial remedy is used.

Administration.—Quinine salts may be given by the following routes

1. Oral
2. Intramuscular
3. Intravenous.

Each route has its own clearly-defined inc
administration.

Certain other methods of adminis
etc., are seldom used and will not be

* But see note on paludrine (p.

Oral Administration.—Quinine is best given as a *mixture*, the sulphate being the cheapest, most suitable, and most generally used salt for routine use. It is a mistake to recommend one of the more soluble salts such as *the bisulphate or the bihydrochloride* on the plea that it is, on account of its greater solubility, more easily absorbed, since all salts of quinine, however given, are reduced to the base in the duodenum before absorption into the blood stream.

Suitable mixtures for routine administration are :—

Quinine sulphate	gr. 10
Dilute sulphuric acid .. .	*min* 10
Water	to 1 oz
	1 oz. t d.s.

or

Quinine sulphate	gr. 10
Citric acid	gr. 30
Mag sulph	gr. 30-60
Water	to 1 oz.
	1 oz. t d s

The individual dose should seldom exceed gr. 10 and the daily dosage gr 30.

Quinine should always be given, where practicable, as a mixture in preference to tablets or powder. It is found only too often that tablets, *especially of the sulphate, are passed unchanged in the fæces.*

If, for any reason, tablets must be given, one of the more soluble salts such as the hydrochloride or bisulphate is preferable in uncoated form.

Whereas, formerly, it was the practice to give prolonged courses of quinine extending over several weeks or even months, with the mistaken idea that relapses might thus be prevented, or at least their incidence materially decreased, it is now realized that such prolonged courses influence the relapse rate but little.

The modern practice is to administer quinine in adequate dosage (*i e.* [illegible] usually for a total of [illegible] ourse of

[illegible]n addition to the above, especially when [illegible] are under[illegible]ing active operations in highly malarious districts, the initial course is followed by a maintenance dose of mepacrine 0 1 g. daily, which is taken regularly by all troops in the malarious area and for one month after they leave it.

Quinine, administered by the mouth, is rapidly absorbed in the vast majority of cases, and this is undoubtedly the best routine method of *administration and should invariably be used in the absence of the special* indications noted below for intramuscular or intravenous administration.

Intramuscular Injection—The bihydrochloride of quinine (Rogers recommends the bihydrobromide) is the salt usually used on account of its solubility (1:1 in water).

[illegible] injected deep [illegible]

part of the buttock that can be seen when the patient is sitting is free from this danger this does not mean to say, of course, that the patient should sit up to receive his injection; he is usually too ill for this to be safe or, indeed, possible.

The chief indications for intramuscular administration may be tabulated thus —

1 Quinine cannot, for any reason, be swallowed

2 Retention of quinine swallowed is doubtful owing to nausea or vomiting.

3 Failing a satisfactory response to treatment, quinine cannot be demonstrated in the urine and its absorption is doubtful

4 A heavy blood infection, especially important in subtertian infections, *i e.* more than 6 parasites per thin field of a blood slide; even in the absence of a severe clinical attack of malaria.

5 In all severe, especially *pernicious*, malarial attacks

In addition to the above well-recognized indications it may be advisable, in some areas where subtertian infections are known to be unduly severe, to give *all* cases infected with *P falciparum*, even if clinically mild and not showing a heavy blood infection, a few preliminary intramuscular injections before proceeding with the routine oral administration.

There are certain drawbacks to intramuscular injection. These may be briefly summarized —

1. It is apt to be painful This is not usually the case if properly carried out, rigid asepsis maintained, and the sciatic nerve area avoided.

2 It may leave indurations lasting for years

3. Some necrosis of tissue invariably follows intramuscular injections of quinine. Occasionally, especially in the case of debilitated individuals or if the technique has been faulty, an abscess forms which may lead to extensive sloughing, prolonged invalidism, and even endanger life

4 Tetanus, due either to autogenous infection or to the introduction of spores at the time of injection, is a rare sequel

In spite of the above somewhat formidable array of objections, intramuscular injections are regularly given without ill-effect, and one should never hesitate to use this method if faced with any of the indications mentioned above.

On the other hand, intramuscular quinine should never be used merely as an alternative to oral quinine, nor should it be continued a day after the special indications mentioned above have been brought under control, when the course may be completed by the oral route

Intravenous Injection.—Quinine is given by the intravenous route when, for any reason, a very rapid concentration of the drug in the blood stream is considered advisable, or if the patient's condition is considered to be so bad that administration by other routes is unlikely to be followed by absorption.

It is indicated in some of the more urgent pernicious attacks, especially

algid and *cerebral* malaria, both of which constitute grave medical emergencies.

Many consider that the indications for intravenous quinine are the same as for the intramuscular route, and always give the former in preference.

They claim the following advantages :—

1. Absence of pain.
2. Absence of necrosis of tissue and its sequels, gluteal abscess and prolonged invalidism.
3. Rapid action.
4. Absence of tetanus as a sequel.

The following drawbacks to intravenous injection may be noted :—

1. Intravenous quinine depresses the circulation and may further lower the blood pressure in an already severely shocked patient.
2. Fatalities occasionally directly follow its use.
3. The rapidity of its action may in itself constitute a danger, a large number of parasites suddenly being destroyed and the toxic products of their disintegration thrown into the general circulation (a variety of Herxheimer reaction).

Quinine bihydrochloride is the salt usually chosen for intravenous injection. 8–10 grains are dissolved in 200 c.cm. of warm sterile saline solution and infused into the vein at the bend of the arm; or the same dose may be dissolved in 20 c.cm. and injected very slowly from a syringe. In collapsed cases an intramuscular injection of 10–15 minims of adrenaline hydrochloride 1/1000 may be given before the intravenous quinine. Adrenaline or pituitary extract should be ready at hand for emergencies. The intravenous injection should be repeated if the patient is still unconscious after 6 hours, but oral quinine should be instituted directly the special indications necessitating intravenous or intramuscular quinine have ceased to operate.

Other Quinine Preparations.—A number of proprietary preparations, many of them containing a quite insufficient quantity of quinine, are on the market. Among these may be mentioned the following :—

Esanophele.—An Italian quinine-arsenic preparation; each tablet contains gr. 1/3 quinine bisulphate, gr. 1/100 arsenious acid, and gr. 2/5 iron citrate. The adult dose is 6 tablets (containing gr. 2 quinine) daily. Probably on account of its arsenic and iron content esanophele has proved useful in the treatment of chronic relapsing malaria.

Bacelli's mixture.—Contains rather more quinine sulphate which is combined with iron and arsenic. The dose is 30 c.cm. t.d.s. Both the above are popular continental remedies.

Quinio-stovarsol and *quinine troposan* (troposan is an isomer of stovarsol), constitute a convenient method of giving quinine in association with arsenic.

Stovarsol has a definite therapeutic action on *P. vivax* infections, but has little effect on infections due to *P. falciparum* or *P. malariæ*. It has

therefore to be combined with quinine as a general therapeutic agent in malaria.

The dose of quinio-stovarsol is gr. 4 (1 tablet) 4 times a day. The daily dosage contains gr. 8 of quinine.

Tebetren is a proprietary drug containing hydroquinine (closely allied to quinine), acriflavine (an acridine derivative with no specific action on the malarial parasite) and bile salts which are supposed to act as a detoxicating agent.

The active principle of this British preparation is hydroquinine, and its therapeutic indications and limitations correspond closely with those of quinine

Malarcan has a similar action to tebetren, but contains hydroquinidine in place of hydroquinine.

Cinchona febrifuge is an impure mixture of all the alkaloids present in cinchona. It is considerably cheaper than the quinine salts and is, on that account, suitable for village use It is very insoluble and is best given as a powder, the dose being the same as for quinine. The drawback of the preparation is that its alkaloidal and quinine contents are not standardized and, whilst some samples are potent, others are almost inert.

Totaquina, a refined modification of the above recommended by the Malaria Commission of the League of Nations, is standardized to contain not less than 70 per cent. total alkaloids of which 1/5th must be quinine.

Toxic Effects of Quinine.—The administration of quinine is attended ith little risk and close medical supervision is seldom necessary

Certain characteristic side-effects are, however, observed when the oncentration of quinine in the blood reaches a certain point These re grouped under the term, *cinchonism*, and consist of deafness and uzzing or ringing in the ears, slight giddiness, and tremors, the first wo, especially, occur in a considerable proportion of those taking quinine n therapeutic doses, are of little importance, and subside rapidly when he drug is discontinued.

Very rarely, definite idiosyncrasy to the drug is met with, and some few ndividuals develop an alarming train of symptoms of an allergic type after ven small doses (gr. 1 or less) of quinine These toxic symptoms vary rom case to case, but include urticaria with marked itching, skin hæmorrhages, dyspnœa, œdema of the eyelids and elsewhere, and dangerous or ven fatal collapse.

In the past such individuals have either been debarred from living in a nalarious district or have lived there at their peril Various substitutes vere used, notably quinidine, an isomer of quinine, but unfortunately this lrug is not free from risk. Luckily, nowadays, we possess in mepacrine n effective and harmless substitute

Apart from the above, excessive dosage (as much as gr 180 daily has been given in the past by some misguided enthusiasts) may lead to permanent blindness due to quinine amblyopia, and to permanent internal ear deafness.

Quinine Resistance.—Some authorities have suggested that certain strains of malarial parasite may become "quinine resistant" after prolonged medication, as the trypanosome has been shown to become resistant to certain arsenical preparations.

There is a lack of controlled evidence to support this hypothesis, and it may be assumed as a working rule that if an attack of malaria fails to [illegible]

[illegible] cause than malaria for the prolongation of the fever and symptoms must be sought.

Synthetic Anti-malarial Drugs.—Two synthetic anti-malarial remedies, [illegible]

[illegible] and the same limitations as quinine and can be used as an alternative to the latter.

Pamaquin, on the other hand, differs from both quinine and mepacrine in these two respects, and can never be used as a substitute for them, rather is it complementary in its action to these two drugs.

Sulphonamide drugs have some action against malaria parasites, especially *P. falciparum*. They are much less effective than quinine or mepacrine, their future status as anti-malarials will depend on whether more effective compounds can be discovered.

Paludrine.—*See* note on p 353.

Paludex is a proprietary oxyquinoline preparation of Belgian manufacture. J. C. Niven carried out exhaustive trials on subtertian malaria with this drug and concluded that it was an inefficient remedy.

Penicillin is *not* an anti-malarial drug.

Mepacrine.—This drug belongs to the acridine series. It was first synthesized by German chemists and marketed by Messrs Bayer under the name of *Atebrin*. The drug and drugs closely allied to it have since been manufactured in a number of countries. *Mepacrine* is the British equivalent of atebrin, in the U.S.A the terms *atabrine* or *quinacrine* are employed *Quinacrine, Acriquine, Haffkinine* and *Crinodora* are the names used in other countries for similar preparations.

Mepacrine is available in three forms.—

(*a*) *Mepacrine hydrochloride* (atebrin hydrochloride of Bayer), a yellow powder sparingly soluble in water. It is generally marketed as a tablet containing 0 1 g. of the drug.

(*b*) *Mepacrine methane-sulphonate* (Atebrin musonate of Bayer) is a soluble preparation for injection. It also is a yellow powder and is put up in ampoules containing 0 375 g. mepacrine methane-sulphonate which amount is equivalent to 0 3 g. mepacrine hydrochloride. It is suitable for intramuscular injection.

(*c*) *Mepacrine dihydrochloride*, a soluble American preparation, is now also available for parenteral use. For this purpose it is put up in specially-marked ampoules.

Action of Mepacrine.—Mepacrine has an active *schizonticidal* action on all varieties of the malarial parasite and is therefore useful in the treatment of the acute malarial attack (*see* Fig. 44 A–E).

It has a poor *gametocidal* action, especially on the crescents of subtertian malaria. It has also little effect in reducing the relapse rate, especially of benign tertian malaria, but it is better than quinine alone It is the best drug so far found both for suppression and treatment of *P. falciparum* malaria. The selective action of mepacrine and quinine on the malarial parasite will thus be seen to be almost identical, especially in benign tertian infections.

Mepacrine has certain *advantages* over quinine, namely —

1. It is not unpleasant to take and has not the bitter taste of quinine (an important consideration with soldiers)
2. It is effective in tablet form which renders its administration easy.
3. Only a small minority of patients suffer from such minor side-effects as gastro-intestinal irritation, slight headache, depression, etc. These are less pronounced than the tinnitus, deafness, nausea, etc, often associated with quinine.
4. Those with an idiosyncrasy to quinine can take mepacrine with impunity. Mepacrine appears to provoke no similar condition
5. The onset or threatened onset of blackwater fever is no contraindication to mepacrine treatment.
6. Mepacrine is excreted from the body more slowly than quinine, it therefore retains its therapeutic action for a longer time after cessation of treatment This is of special application in malaria suppression

Mepacrine has certain *disadvantages*, viz :—

1. Mepacrine, given by mouth, appears to exert its action on the initial pyrexia of the malarial attack more slowly than quinine For this reason some authorities advise a preliminary two days' course of a quinine mixture before commencing the routine mepacrine course (*see* Fig 44C)

   There is evidence that if mepacrine is given in relatively large doses (*i e.* 0 2 g six-hourly for the first 48 hours, followed by a maintenance dosage of 0 3 g daily for seven to ten days) cases thus treated respond as rapidly as those on quinine This (or even heavier dosage) ensures that an effective blood concentration of the drug is attained early in the treatment of the disease
2. Some individuals, during or shortly after a course of mepacrine, develop a yellow discoloration of the skin, due to the excretion of the dye into the dermis and *not* due to jaundice An important point of distinction is that whereas in jaundice the sclerotics are almost invariably tinged yellow at an early stage—before the skin is yellow—in discoloration due to mepacrine the skin is usually tinted a definite yellow before the conjunctivæ, which, if stained at all, are only very slightly discoloured by the drug. The skin discoloration may persist for many weeks (up to sixty-nine days).

3. A rare complication, usually occurring at the end of a course of mepacrine, is a transitory psychosis of the acute confusional (toxic) type, which rapidly disappears after cessation of treatment.

Methods of Administration and Dosage.—Mepacrine hydrochloride may be given by mouth in tablet form, two 0·1 g. tablets four times a day for two days, thereafter one 0·1 g. tablet three times daily for six to eight days. *This is a suitable dosage for the treatment of an adult male* suffering from any form of uncomplicated malaria. For women and children the dose should be reduced.

[illegible]

the muscles of the buttock.

One to three injections at intervals of twenty-four hours are usually *sufficient, the full course being completed by the oral route.*

Alternatively, mepacrine dihydrochloride, a standard American preparation for parenteral use may be used, the dose is 0·2 or 0·4 g. intra*muscularly in 10 c.cm. or 20 c.cm. of sterile distilled water. If necessary* up to two doses may be given daily for several days. As a rule, one or *two injections suffice; the rest is given by mouth.*

[illegible]

muscular injection is extremely rapid; intravenous injection is contraindicated.

The indications for intramuscular mepacrine are the same as for intramuscular quinine (*see* Fig. 44D).

It is an open question whether intramuscular mepacrine can replace intravenous quinine in the urgent treatment of cerebral and algid malaria. Until more data are available it is probably safer to use *intravenous quinine, either alone or in combination with intramuscular mepacrine, for* these grave medical emergencies

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[illegible] entary
to that of quinine and *mepacrine;* it can, therefore *never replace* these drugs, but may be employed, usefully, to supplement their action.

[illegible] has there-
[illegible] r be used
[illegible] k. It has
a marked *gametocidal* action, especially on the crescents of subtertian malaria. These break up and disappear after a very few doses of the drug, whereas their numbers are little if at all affected by quinine or mepacrine

Most important of all from the therapeutic standpoint, pamaquin has a marked effect on the relapse rate, especially of benign tertian *malaria.*

supervision in hospital.

It is suitable only for oral administration

The chief toxic manifestations are —

1 Epigastric pain of a dull aching character and of obscure causation.

2 Cyanosis, unaccompanied by dyspnœa or cardiac distress, due to methæmoglobinæmia

The above symptoms, alone or in combination, occur in a small proportion of susceptible individuals even when on minimal dosage; they usually disappear after withholding the drug for a few days and do not, in most cases, recur if the pamaquin is now readministered These symptoms occur, most commonly on the sixth to ninth day of administration; coloured races are most susceptible.

Other much rarer toxic manifestations are hæmoglobinuria, resembling blackwater fever, hæmolytic jaundice, and acute yellow atrophy, leading in rare instances to death

Indications for Treatment —Pamaquin should be given *not* during the acute attack of malaria, but at the termination of a short course of quinine or mepacrine, when the fever has been brought under control and gametocytes are to be expected in the peripheral blood. Dosage 1 pamaquin tablet, each 0 01 g, thrice daily for three to five days or up to ten days in special anti-relapse courses.

Pamaquin given along with quinine (quinine grains 10 and pamaquin 0 01 gramme thrice daily) in a ten-day course has a marked effect on the subsequent relapse rate of benign tertian malaria In very chronic and non-responding cases the above course may be extended to 21 days (*see* Recommended Malarial Courses below).

It is of historic interest that this quinine-pamaquin course was used at the Malaria Treatment Centre, Kasauli, N India, as early as 1928, when it was found to be of the greatest use in cutting down the relapse rate of B T. malaria

Recommended Malarial Courses

A *Standard Quinine-Mepacrine-Pamaquin (QMP) Course*, suitable for routine treatment of primary attacks and of first and second relapses of all varieties of malaria. This course was in general use in several theatres —including the Middle East—during the first three years of the 1939–45 war, but it has now been largely superseded by course B —

(1) Quinine, grains 10, given as a mixture thrice daily for two or three days or until the temperature has dropped to normal.

(2) Mepacrine, 0 1 gramme thrice daily for five to seven days.

(3) Two days' rest period without drugs. (This rest period can be omitted)

(4) Pamaquin, 0 01 gramme thrice daily for three to five days.

B. *Mepacrine (M) Course.*—An improvement on A.

Days 1 and 2, Mepacrine, 0 6 to 0 8 g as a total daily dose; to be given in three or four divided doses.

Days 3–5, Mepacrine, 0 1 g thrice daily.

This dosage should be reduced for Indian troops, for women, and, of course, for children

C. *Quinine-Pamaquin (QP) Course.*—Suitable for cases which have relapsed more than twice after exposure to reinfection has ceased.

Quinine, grains 10 Pamaquin, 0 01 gramme	*thrice daily for 10 to 14 days.*

(Indian and other troops of light weight should receive pamaquin 0 01 g. twice instead of thrice daily.)

D *Prolonged QP Course.*—An extension of course C, suitable for chronic cases which have relapsed many times after exposure to reinfection has ceased

Quinine, gr. 10 Pamaquin, 0 01 g	thrice daily for seven days
Quinine, gr. 10 Pamaquin, 0 01 g.	twice daily for fourteen days.

—0 1 g

elapsing

(Continued on page 191)

Explanation of Figs 44 A–F in pages 192–197.

During the malaria "rush" season there may be little time or opportunity for the preparation or keeping up to date of elaborate case records of individual cases of malaria. Much valuable information may thus be lost.

In these circumstances many important details, both clinical and pathological, may be incorporated in the individual temperature charts, which are collected when the case leaves hospital and stored for future ... of the malaria season when records have

be

(*a*) Result of daily examination of blood films (thick). (Symbols used.—M.P.=malarial parasites in peripheral blood; G=gametocytes, C=crescents.)

(*b*) *Condition of spleen day by day. (Symbols used*—*T.=tender* but not palpable spleen; B P.=barely palpable spleen, P.=palpable spleen; P.1=one-finger spleen, P.2=two-finger spleen, etc.)

(*c*) *Any outstanding symptom with date of onset:—i.e. epistaxis, coma,* malarial dysentery, etc.

(*d*) Any specific treatment employed and method of administration if ... I.V. = intravenous). In

d

Explanation of Figs 44 A–F *in pages* 192–197 (*continued*)

If standardized and routine treatments are used they may be indicated at the top of the chart In these examples:—

A = Standard course of atebrin (mepacrine).

A + P = Atebrin (mepacrine) followed by plasmoquine (pamaquin) in standard dosage.

A.P. = Atebrin and plasmoquine given together in combined dosage. (This is *not* now advised.)

Q = Quinine; T = Tebetren, etc, etc.

Concise and systematized records such as these, especially if used in conjunction with the Malaria Register (which records such details as the date of onset; when and where infected, date and number of previous attacks, etc, etc.), will prove of great value when consolidated records have to be written up

Note.—Mepacrine and pamaquin should *never* be given together, *i.e concurrently*, either in one pill (a combined pill is marketed called Atape) or in separate doses They should always be given *consecutively*, mepacrine first, preferably followed by two days' rest, then pamaquin

The toxic effects of both drugs appear to be enhanced by their administration together (*see* Fig 44F)

This objection does not operate in the case of combined quinine and pamaquin.

If any evidence of pamaquin intolerance appears such as epigastric pain, cyanosis (methæglobinæmia), or other untoward signs of symptoms, pamaquin therapy should be discontinued at once and only the quinine course completed. The treatment of pamaquin hæmoglobinuria is the same as that of blackwater fever.

(*Continued from page 190*)

General Treatment.—The diet should be fluid until the paroxysm has subsided. Plenty of fluid should be given to combat dehydration due to excessive sweating If dehydration is extreme a rectal or intravenous saline may be necessary and should not be delayed until it is too late.

If there is hyperpyrexia, *i.e.* a temperature of 105 F or over, the patient must be tepid-sponged and, if necessary, douched or bathed as for heatstroke (*see* p. 131)

In severe cases with marked jaundice, as in the form of malaria known as bilious remittent fever, plenty of sugar should be given in the form of sweetened drinks, or as glucose by the bowel or by intravenous injection in a 5-10 per cent solution. Vomiting, which may be severe and obstinate, may tax all our therapeutic resources Adrenaline hydrochloride, 20 minims of a 1:1,000 solution in half an ounce of water, given hourly until the vomiting stops, is often an effective remedy Sips of iced champagne may act like a charm, especially in nervous women The essential remedy is usually to treat the malaria with appropriate and adequate parenteral therapy.

Fig. 44A.

Case of B T (benign tertian) malaria treated with mepacrine 0·1 g t d s for 6 days, follow… after two days' rest, by pamaquin 0·01 g b d for 5 days

Fig 44B

Case of quartan malaria treated with an eight-day course of mepacrine (0 1 g t d s.), with a rest period of two days after the sixth dose

This treatment is effective as far as the individual attack of malaria is concerned, but the omission of pamaquin entails a high relapse rate

Fig. 44C.

M T malaria Slow response to oral mepacrine A few initial doses of a quinine mixture or of intramuscular atebrin, or a higher dosage of mepacrine would have produced a more rapid result

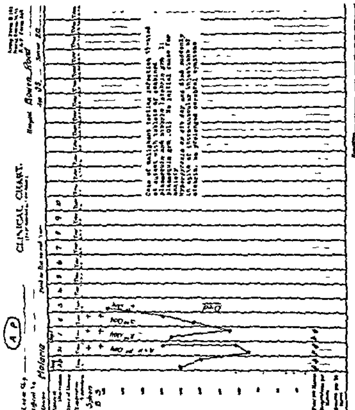
Fig. 44D.

Severe M.T. malaria treated by three initial intramuscular injections of mepacrine at daily tervals, followed by oral quinine to complete the six-day course, this being followed after a rt period of two days by a five-day course of pamaquin (0·01 g. b.d.)

Fig. 44E.

Case of mixed M.T. and B.T. infection. Rapid response to mepacrine, first dose intramuscular injection.

Fig. 44F.



Patient with M.T. *malaria* who died suddenly while under treatment with tablets containing atebrin and plasmoquine in combination. These tablets are not now used

had to avoid. Another point is that manpower was conserved and lives saved by spectacular reduction, not only of malaria rates, but of all pernicious manifestations. Blackwater fever became a rare disease in West Africa—an almost incredible victory to those who were best informed about this part of the world.

It must be emphasized that the administration of suppressive treatment does not imply that other methods for the prevention of malaria may be relaxed, on the contrary the fact that suppressive treatment has been found necessary is to be taken as a reminder that the area is highly malarious and that all other precautions must be carried out and anti-malaria discipline tightened up to the greatest possible degree.

General principles governing the Use of Curative and Suppressive Drugs among Soldiers

During the 1939–45 war we learned a lot that was new, but many are still uncertain how our knowledge can best be applied to the therapeutic control of malaria under the varying conditions of war service.

[illegible] great deal of confusion and controversy be[illegible] ma[illegible] defined and the principles of curative and suppressive treatment summarized.

(1) **Gametocyte Prophylaxis** is the prevention of the acquisition of infection by the mosquito because of the action of drugs on the gametocytes or their precursors in the human body.

(2) **True Causal Prophylaxis** is the prevention of the acquisition of infection by the human host through the action of drugs upon the sporozoites injected by the mosquito, or upon any intermediate stage of the parasite between the sporozoites and the asexual blood forms.*

(3) **Suppressive Treatment** is the prevention of the development of the clinical manifestations of sub-patent infection by means of the continued action of drugs on the asexual blood forms.

(4) **Cure.**—The term "cure" is used in a very loose sense by many writers on malarial therapy. It must always be clearly indicated whether the term is intended to mean *radical* cure (a complete eradication of infection), or merely a *clinical* cure (abolition, perhaps only temporary, of those clinical manifestations present when treatment began).

(5) **Radical Cure** is the permanent *elimination of infection* by the [illegible] of all those forms of the parasite capable of continuing [illegible] ry, of the [illegible] r military [illegible] nciples of [illegible] rugs must

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* *See* note on paludrine on p 353

be fully understood and the drugs themselves applied correctly in various circumstances.

The following table (after Sinton) indicates the action of the common anti-malarial drugs against the common parasites —

TABLE

Action of Drugs on Different Stages of the Malarial Parasites

Drugs	Asexual Forms			Sexual Forms		
	BT	Qt	MT	BT	Qt	MT
Quinine	++	++	++	++	+	O
Mepacrine	++	++	++	++	+	O
Pamaquin	+	+	O	++	++	++

Note —BT means benign tertian parasites, Qt, quartan parasites, and MT, malignant tertian parasites. The sign ++ indicates a marked estructive action, + a less-marked action, and O an absence of de-uctive action.

Now that the terms have been defined and the actions indicated, principles and recommended courses (*see* p 189) may be summarized follows —

A *Non-infected individuals coming to reside in an area where the chance of acquiring malarial infection are slight*

(a) *Suppressive treatment.* None.

(b) *Primary acute attacks* Rapid clinical cure with course of short duration such as Course B or Course A

(c) *Relapsing infections*

(i) Repeat Course B or A.

(ii) Special treatment for chronic BT or Qt (Course C or D)

B *Individuals coming to reside in a non-malarious or slightly malarious region from one that is highly malarious*

(1) *If the period of absence from heavy risk of infection is likely to be of long duration.*

(a) *Suppressive treatment* Stop suppressive treatment after four weeks (except perhaps among certain key men)

(b) *Primary acute attacks.* Course B or Course A. This will give rapid clinical cure and, in a proportion of men, radical cure

(c) *Relapsing infections*

(i) Repeat Courses B or A (no maintenance)

(ii) Special treatment for chronic BT or Qt (Course C or D).

(2) *If the period of absence from heavy risk of infection is likely to be of short duration*

(a) *Suppressive treatment* Continue suppressive treatment without any cessation

(b) *Attacks.* Treat attacks to produce a rapid clinical cure (Course B is best) and follow this treatment by suppression without any interval (maintenance of treatment).

C. *Individuals exposed to constant and frequent infections, reinfections, and superinfections.*

(1) *Immune or "salted" populations.*

(a) *Suppression.* If much malarial sickness occurs, start mepacrine suppression in moderate dosage; this can often be stopped after a few months.

(b) *Attacks.* Treat attacks to produce a rapid clinical cure—not radical cure.

(c) *Gametocyte prevention.* Gametocyte therapy with three or four doses of 0 01 g. of pamaquin or light suppressive treatment is sometimes necessary to prevent spread of infection to adjacent non-immune troops.

(2) *Non-immune or semi-immune troops.*

(a) *Suppression.* Continuous suppressive mepacrine should be given in full doses even if there is a break in the malaria transmission season (*see* B.2).

(b) *Attacks.* Give short intensive treatment to produce a rapid clinical cure (Course B is best), and follow this immediately *by continuation of full doses of suppressive mepacrine*

Effects of mepacrine suppression.—The following summary (after Sinton) gives a useful outline of the results to be expected from mepacrine suppression. *It will be particularly useful for medical officers who may have to explain to combatant officers what influence suppressed or latent malaria will exert on military problems.* They will be justified in taking the line that there is conclusive evidence that:—

(1) With proper enforcement of mepacrine suppressive treatment a force can maintain itself for many months in the field with a relatively low malarial incidence; this is possible under conditions where, without mepacrine suppression, the disease would put the force out of action within a few weeks.

[illegible] treatment for four weeks [illegible]

(3) The great military value of the immediate effects of suppressive treatment should not be minimized, but it must be remembered that these later attacks may have very serious repercussions upon the manpower situation. At present no therapeutic measure is known that will prevent the liability to these late outbreaks, and officers must be warned to expect them. They are especially probable when troops who have been exposed to infection are called upon to operate at the season when such late attacks are likely to reveal themselves. In one such formation—of whom it was

reported that, during the previous malaria season, their "unit discipline was non-existent"—a large number of such late attacks appeared at a critical moment—just before the invasion of Europe (1944)—and gave rise to very serious anxiety.

(4) The use of suppressive treatment must *never* be considered as justifying any relaxation in the enforcement of personal-protection measures against the bites of infective mosquitoes. Indeed, when conditions demand the use of suppressive treatment, this is a sure indication that the chances of acquiring infection are very great. Suppressive treatment, then, so far from justifying a relaxation of personal-protection measures, is one of the surest indications for their strictest enforcement

(5) The evidence that has accumulated during the 1939–45 war again emphasizes that, while the medical services can do—and have done—a great deal to mitigate and remedy the effects of malarial infections, serious conditions may arise, both at the time and at a later date, because of circumstances over which the medical services have no control. These serious conditions are created by failure to enforce anti-malarial orders in the very strictest manner, and, above all, by neglect of those measures of personal protection that are matters of unit discipline. (*See* Control of Mosquitoes under Arthropod Pests, and Appendix *I*.)

(6) The use of mepacrine as a suppressive of malaria (0 1 g daily) is a safe procedure without danger to health.

MYIASIS

This condition, the presence of parasitic dipterous larvæ in the body, is usually classified, according to the site of the lesions, into cutaneous, nasal, intestinal, etc., varieties. Patton's division, based on the breeding habits of the diptera concerned, is much more satisfactory. He recognizes three groups of myiasis-producing flies—Specific, Semi-specific, and Accidental

1. *Specific*, where the larvæ can develop in living tissues only. Examples of this group are *Chrysomyia bezziana*—the commonest cause of human myiasis in India, *Cordylobia anthropophaga*, the well-known Tumbu fly of Africa (see Plate 8 and below), and the Œstridæ, Bot or Warble flies

2 *Semi-specific*—flies which breed normally in decomposing matter, but may occasionally attack living tissues being attracted by foul discharges, blood, etc. Among such flies are *Chrysomyia megacephala* (*dux*), the common Indian bazaar fly, *C macellaria* the American screw-worm fly, several species of *Lucilia* and certain *Sarcophaga*

3 *Accidental*—This group includes flies whose eggs or larvæ are swallowed, usually in food or drink, and develop in the intestine, this occurrence being accidental and no part of the fly's ordinary development.

Blow flies; species of *Sarcophaga*; some Anthomyidæ, especially *Fannia canicularis*, have been found, among others, and one of the Aschiza, *Apiochæta xanthina*, may not only pupate in the intestine, but the adults may even hatch out in this site.

Most of the larvæ causing dermal myiasis do not pierce the skin, but invade wounds, or sores, however small. Some attack the mouth, nose, eyes, ears, or genital orifices, and unless the nature of the trouble is recognized and vigorous treatment applied, there may be great destruction of tissues and even death. Consequently all septic wounds or sores should be effectively protected against flies, particularly in the case of children and helpless people, and those with offensive discharges from the nose or ears should keep the orifice plugged with an antiseptic dressing

Diagnosis.—The diagnosis of myiasis is established by discovery of the larvæ concerned. As there is still much to be learned about myiasis, no effort should be spared to identify the species of fly responsible for the lesions. Kill a few of the mature larvæ by dropping them into "bubbling" water (*i.e.* 80° C., just short of boiling water) and preserve them in 80 per cent. spirit. The remainder of the larvæ should be allowed to complete their development, as this will facilitate identification. The larvæ of specific myiasis-producing flies, like *C. bezziana*, will not develop in dead flesh, but should be placed in a wound on the body of a living animal The larvæ of semi-specific myiasis producers will develop in meat, but this must be carefully protected from contamination by the eggs or larvæ of other flies. Flies may show most uncanny ingenuity in providing for their offspring by dropping eggs, or larvæ, through tiny openings, or depositing them in the neighbourhood of small apertures through which access may be had to meat, etc. Patton has found that the only certain method of excluding contaminating larvæ is to make a secure parcel of the required meat in several sheets of paper. If this becomes damp, further sheets are employed, otherwise foreign larvæ may pierce the softened-paper. The larvæ will pupate in the folds of the paper and the pupæ should then be removed and two or three placed in each of a number of tubes. When the adults emerge they should be kept for a day or two to allow them to harden, and then killed and pinned. For the identification of the various stages of flies concerned in myiasis in India, Patton's invaluable papers on "Indian Calliphorinæ", in the *Indian Journal of Medical Research*, 1920–22, should be consulted, and the diagnosis confirmed by an expert.

Treatment.—Remove the larvæ by douching with chloroform water. Local application of liquid paraffin materially assists extraction. In rhinal myiasis it may be necessary to open the frontal or other sinuses in order to irrigate efficiently. After removal of the larvæ, treat the residual inflammation on ordinary lines.

CORDYLOBIA ANTHROPOPHAGA (Plate 8)

The form of dermal myiasis due to *Cordylobia anthropophaga*, or an allied species, is of sufficient importance from a military standpoint to require a separate note. In parts of the African campaigns of the 1914–18

war this condition was common, and proved troublesome and crippling, especially to the Indian troops.

The fly lays its eggs, as many as 300 at a time, on the ground, dry sand previously contaminated with excreta being favoured. The resulting small larvæ may remain alive for ten days or even longer without food, and are not readily seen unless disturbed. When opportunity offers, the larvæ creep from the sand, soil, etc., on to their hosts. By means of the buccal spine the tiny larvæ penetrate the skin, the actual passage through the epidermis causing little disturbance. When mature they drop out, burrow in the ground and pupate. It is possible that the fly may lay its eggs on clothing, and underclothing, bedding, etc., often transmit infection from the ground. Larvæ placed on cloth may remain alive for at any rate nine days. Infection of the domestic dog is commonly observed, but the most important host appears to be the rat.

Symptoms.—The lesion produced is like a small boil or urticarial weal, in the centre of which there is an opening which may be obscured by discharge or may be patent, when it looks black in colour, owing to the presence of excrement from the posterior end of the larva which may be visible. Pressure on it causes pain. Around the hole the skin is inflamed and very itchy. In East Africa the commonest site appeared to be the forearm, but it is stated that in Europeans the scrotum, upper part of the thighs, and buttocks are most frequently attacked, and it has been suggested that infection takes place when persons are using the latrine. The larvæ may be found in any exposed part, and multiple infections occur. When small they are easily squeezed out, but if neglected attain maturity and may be associated with a little suppuration.

Treatment.—Extract the larva with forceps. This process is less painful if a little chloroform is injected into the larva before its removal. Simple expression is often effective, and is facilitated by free local application of liquid paraffin. Allay the local irritation. Paint the skin with iodine in potassium iodide after the extraction.

NUTRITIONAL DISEASES

Introduction.—Good nutrition is of paramount importance to an army in the field. The nutritional state of troops determines their potential fitness, their capacity to profit from physical training, and their power to overcome hardships and diseases. Nutrition is also a basic factor in morale; only well-nourished troops can show the highest vitality and keenness, especially under adverse conditions.

Accordingly military men have paid great attention to modern nutritional science. Questions affecting the quantity and quality of rations have been intensively studied and a careful analysis has been made of all foods used and likely to be used as rations. From this work much useful information has emerged and elaborate tables have been prepared. Intensive study has also been made of the accessory food factors or vitamins.

Military considerations.—It is stressed that the quality of the field [illegible]

fundamental importance and as true today as when they were first uttered.

Under peace conditions it is seldom difficult to provide a satisfactory and balanced dietary in accordance with a well-designed ration-scale. In war, especially in "total" war, almost unsurmountable difficulties may arise.

An additional problem in war is that many of the intake, especially native recruits, are of poor nutritional standard. Sometimes men are of necessity enlisted from a community where grim poverty or famine conditions have prevailed. Unless the army ration contains a good deal more than the bare minimum of essential nutrients, many of these ill nourished recruits will show evidence of masked or overt deficiency disease as soon as they are called on to undertake the strenuous and fatiguing duties inseparable from a soldiers' life in war.

Transport difficulties to distant theatres of war or to localities ill-supplied with rail or road facilities may prevent certain bulky and perishable but essential items of diet from reaching the forward troops; inferior substitutes—if even these are available—must take their place. Unusual stress, exposure, or disease may further complicate the issue.

Medical responsibility.—A heavy responsibility thus devolves on those who have to draw up the ration scales, those who have to provide the food, those who have to transport it where needed, and those whose duty it is to advise commanders on nutritional problems. Practically all medical officers must expect this responsibility sooner or later.

Nutrition no longer has for its primary aim merely to prevent deficiency diseases, which should be little more than a curiosity now that we know their causation and have effective synthetic products at hand to prevent their development, instead, nutrition aims at maintaining the highest potential level of fitness under normal conditions and at preventing any serious deterioration of fitness when conditions are adverse. In fact it is our constant aim to make and keep the soldier "fighting-fit" instead of merely "fit-to-fight". Between these two physical and mental states there may be all the difference in the world—the difference, it has been said, between being "fit-to-kill", and being "fit-to-be-killed".

In order to discharge their duties effectively, all medical officers should make themselves expert in nutritional problems and should be interested in food standards and their rationale; they should be thoroughly acquainted with the make-up of standard ration scales, especially those in use by the troops under their medical care, and they should be in a position to criticize effectively and expertly any modifications of the dietary or any substitution of its various items that may be proposed or introduced under the local conditions of peace or war.

Medical officers must know well the early signs of malnutrition, but they must not be so eager or so misguided as to find these manifestations where in fact they do not exist; they must fully inform themselves of the

mportance of catering and cooking in the maintenance of satisfactory nutrition.

The medical officer may well ask how he can best acquire the detailed knowledge he needs to deal satisfactorily with nutritional ...
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NUTRITIONAL-DEFICIENCY DISEASES

... are also short paragraphs on ...
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... whose etiology is little understood, is probably a conditioned nutritional disorder; it is discussed elsewhere (p 301)

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... is very common in many nutritional disorders—in pellagra, for example, and in starvation with or without œdema. Non-specific diarrhœa was noted in about 50 per cent of semi-starved, repatriated British ... has been claimed that

... and amœbic, is common ... care must therefore be taken, by stool examina-

tions and by sigmoidoscopy if necessary, to exclude dysentery as the cause of the diarrhœa.

Vitamin A.—Vitamin A exists in foodstuffs in two forms: either as preformed vitamin A in animal foods, or as the yellow plant-pigments collectively known as carotene—*the precursor of vitamin A*, which is converted in the animal body into vitamin A itself. Carotene is less readily absorbed and used than preformed vitamin A, so that the vitamin-A potency of plant foods cannot be judged solely by their carotene content. *The chief sources of preformed vitamin A are liver, whole milk and milk* products (butter, cheese, cream), egg yolk, and fatty fish. The liver oils of fish are exceptionally rich in vitamin A, although this is of importance in therapeutics rather than dietetics. Carotene is found in many plant foods, especially the green leafy vegetables and the yellow or red vegetables such as the carrot, tomato, red pepper, and others. Red palm oil, which is used by many native races as a cooking-oil, and was extensively employed in recent desert campaigns to offset the shortage of vitamin A in the diet, is a concentrated source of carotene. Unfortunately cooking destroys much of its power to function in this way.

Serious disorders due to vitamin-A deficiency have been relatively infrequent during the 1939–45 war although many of the dietaries, especially those in use in the most forward desert areas of the Middle East, were notably deficient in vitamin A. But there have been reports of minor

by vitamin-A deficiency.

Eye manifestations.—At one stage of the 1939–45 war, *night-blindness* assumed some importance, especially among R.A.F. crews and troops operating under desert conditions in the Middle East Force. Since the evaluation of this disorder depends largely on subjective (dark-adaptation) tests, it is difficult to make sure that in any given case the condition is not due to or materially aggravated by a psychoneurosis which *is itself* associated with faulty dark-adaptation. It is important to note that few individuals complaining of this defect, which was also prevalent in certain Italian P.O.W. camps, showed any other evidence of vitamin-A or other deficiency.

In India the diagnosis of night-blindness is not encouraged and the term may not be used in front of troops.

Other ocular signs that can be attributed with more certainty to vitamin-A deficiency are due to the metaplastic keratosis of epithelial surfaces which is one of the important effects of vitamin-A deficiency, viz.:—

(*a*) *Xerosis conjunctivæ*, which causes dryness and greasiness of the *conjunctivæ, is readily made manifest if the eyelids are held apart* for a few moments; it also gives rise to vertical wrinkling, most evident in the temporal conjunctiva. In dark-skinned races, there is also described an irregular brown pigmentation of the sclerotics which gives them a smoky appearance.

(*b*) *Bitot's spots* are small but conspicuous white plaques of dried,

keratinised epithelial cells, which lie like flakes of whitewash on the surface of the orbital conjunctiva. Bitot's spots must be distinguished from pterygium (patch of thickened conjunctiva extending over a part of the cornea) and pinguecula (yellowish spots due to old age). Neither of these is in any way related to vitamin deficiency.

Xerosis conjunctivæ and Bitot's spots are not infrequently found among Indian recruits, the incidence showing marked variation in different races

Skin manifestations.—The chief of these, common among Indian and African recruits, is follicular hyperkeratosis (phrynoderma or toadskin) This is most commonly found on the extensor surfaces of the upper limbs but it may also occur on the back, thighs, and buttocks. There is need for caution in making this diagnosis in native recruits or soldiers because their skin is often dry and rough quite apart from any vitamin-A deficiency

It is emphasized that Bitot's spots and follicular hyperkeratosis are chronic manifestations involving structural changes in tissue and requiring intensive and prolonged therapy for their relief Their presence does not necessarily imply that the individual's diet is short of vitamin A at the time of the examination Their military significance must be carefully and sensibly assessed, it is often nil

Vitamin B.—The vitamin-B complex contains three main components necessary to the human economy .—

Thiamin (vitamin B_1, aneurin).—Deficiency causes beriberi

Riboflavin (vitamin B_2, lactoflavin).—Deficiency causes a mixed syndrome, often called ariboflavinosis.*

Nicotinic acid (niacin).—Deficiency causes pellagra

The following optimum requirements have laid been down by the National Research Council of America for the three components of the vitamin-B complex in relation to total calorie intake —

Calorie value of diet	Thiamin (mg)	Riboflavin (mg)	Nicotinic acid (mg)
2,500	1 5	2 2	15
3,000	1 8	2 7	18
4,500	2 3	3 3	23

It must be noted that the *optimum*, probably also the *minimum*, daily requirements of the vitamin-B complex are not expressed as a "flat-rate" but as a rising scale that increases in relation to the total food intake and to the energy output of the individual.

Although beriberi and pellagra, which are discussed in detail elsewhere, are the best-defined entities of the complicated vitamin-B complex deficiencies, it is generally recognized that deficiency of more than one

* "Riboflavin deficiency" is a more accurate term than "ariboflavinosis", which ought to mean complete absence of riboflavin

strain—both physical and mental—may act as important *trigger-mechanisms* if the vitamin content of the food, and consequently of the tissues, is at a low level.

Riboflavin (*vitamin* B_2, *lactoflavin*) is one of the most recently differentiated members of the vitamin-B complex. The signs and symptoms caused by its deficiency in the food and tissues are still on a somewhat controversial plane and have not yet been completely sorted out.

The chief sources of riboflavin are: yeast, wholemeal cereals, pulses and nuts, milk, cheese, eggs, lean meat, and liver.

The healthy adult is said to require 2–3 mg. of riboflavin daily; a diet containing only 1 mg daily caused an overt outbreak of riboflavin deficiency during the 1939–45 war.

Among the chief symptoms attributed on good evidence to lack of riboflavin in the diet are: glossitis of rather a special type, angular stomatitis, and cheilosis.* A fine, branny, desquamating, and irritating scrotal dermatitis has been an inconstant symptom. Corneal vascularisation, considered by many authorities to be a very constant sign of riboflavin deficiency, has been absent in most of these cases.

An excellent description of the changes in the mouth and pharynx that are due to riboflavin deficiency is given in the *Field Service Hygiene Notes*, page 101, para. 154 (India, 1945). It is given here, almost word for word:—

> *Tongue changes* occur in vitamin-B_2 deficiencies. They are common also in certain other diseases, such as sprue and macrocytic anæmia, [illegible]
>
> colour. The centre of the tongue was usually covered with thick white fur. In the second stage, the tongue was completely stripped of fur and was smooth but not glossy; it was slightly swollen, with lateral [illegible] æ were flattened. Fissur- [illegible] fissures ran longitudinally [illegible] which looked as though [illegible] -ss or burning on taking food was reported in some cases, but subjective symptoms were surprisingly few having regard to the physical signs. This condition of the tongue is very suggestive of riboflavin deficiency if it is found in association with one or more of the following: angular stomatitis, [illegible] nd [illegible] -d, [illegible] ci- [illegible]
>
> *Angular stomatitis* consists of transverse fissures at the corners of the

* In introducing the term cheilosis (redness, desquamation and ulceration of the lips), Sebrell described a condition which included angular stomatitis, but many writers today use the terms separately.

mouth, with maceration and possibly encrusted exudation. At an early stage there may be simply a white sodden epithelium without fissuring.

Cheilosis may also be present—redness, desquamation, and finally ulceration along the mucous membrane of the lips. Among troops showing the tongue- and mouth-signs of riboflavin deficiency, it has been observed that the soft palate is more or less injected, and a sharp demarcation line appears between the red soft-palate and the white hard-palate.

Sore throat, dysphagia, hoarseness, and aphonia were among the first reasons given for reporting sick during an outbreak of riboflavin deficiency among Indian troops. These symptoms disappeared rapidly under treatment with marmite or pure riboflavin.

OTHER SIGNS OF B-COMPLEX DEFICIENCY

Besides the changes already described, there may be seborrhœa of the nasolabial folds and malar regions with branny desquamation. Failure of vision, although admittedly of obscure origin, has also been attributed to B-complex deficiency. A separate note on this condition is required.

Failure of Vision.—A nutritional disorder with progressive failure of vision was described during the 1939–45 war from various parts of the world. The most usual early complaint was of increasing difficulty in reading. One limited outbreak of this type occurred in the Middle East and another in prisoners liberated from the Far East.

The disorder occurred chiefly among ill-nourished communities with a history of pellagra or allied deficiency. The presenting symptom was failing vision which might progress to complete blindness. The chief ocular signs were: pallor of the temporal halves of the discs, occasionally progressing to optic atrophy, varying degrees of peripheral constriction of the visual fields, and, in at least one series, a characteristic central or paracentral scotoma. Retrobulbar neuritis was regarded as the underlying lesion.

In addition to the failure of vision, there were other nerve signs in the same group of men. Unilateral or bilateral nerve deafness was a common complaint and a third of one series of patients complained of unsteadiness of the lower limbs with exaggerated leg reflexes and diminution or loss of vibration- and joint-senses. Rombergism was common. A few who complained of voice changes were found to have paralysis of one or both vocal cords. A minority showed memory defects. Other findings were hypochromic anæmia and hypo- or a-chlorhydria. Several gave a history suggestive of riboflavin deficiency (angular stomatitis, glossitis, irritating scrotal dermatitis). All who were interrogated had suffered from at least one attack of dysentery. Yeast and nicotinic acid proved effective remedies in those without irreversible optic-nerve changes, but riboflavin was more effective than either.

Vitamin C (Ascorbic acid).—The richest sources of vitamin C are the citrus fruits (especially lemons), tomatoes, and most green vegetables.

Care must be taken in cooking since vitamin C is readily destroyed by heat especially in the presence of alkali.

Deficiency of vitamin C causes increased capillary fragility and bleeding If the deficiency is severe and sufficiently prolonged, there develops the clinical syndrome known as scurvy.

Scurvy

Scurvy was rare among the Allied forces during the 1939–45 war although it was common enough among recently-captured enemy prisoners of war The reasons for our virtually-complete immunity from what was formerly a scourge of armies in the field are quite clear excellent arrangements were made for the supply of fresh vegetables and fruit, often under conditions of the greatest possible difficulty Where deliveries of such supplies were impossible for transport or other reasons—under siege conditions, for example—the large-scale provision of ascorbic acid tablets was an effective substitute But occasional cases are bound to occur, sometimes when least expected, and they must be looked for.

Scurvy usually begins insidiously. Early symptoms are. loss of weight, progressive weakness, pallor, stiffness of the leg muscles, and, occasionally, formication in the soles of the feet. Later, the gums are affected, the earliest sign being soft, bright-red swellings or "buds" *between* the teeth (Plate 30) These "buds" become "blossoms" which spread and unite; the gums become swollen and spongy; ulceration and bleeding follow. As the disease progresses the teeth become loose, in extreme cases, now rarely seen, the gums present large fungating masses that push out the cheeks The tongue becomes swollen and the breath foul, the salivary glands may enlarge.

Hæmorrhages under the buccal mucosa and elsewhere are common Petechial hæmorrhages round the hair-follicles of the thighs, arms, and trunk, are an early but important sign. Hæmorrhages tend to occur in the muscles which have most work to do—in soldiers, the leg muscles It is suggested that the condition of *tropical pyomyositis*, which is common among some groups of African recruits, may be due to the invasion of these intramuscular hæmorrhages by pyogenic cocci.

Hæmorrhages around or near a joint may interfere with its movements. Subperiosteal collections of blood are usually a late symptom. They are found especially over the tibia and along the costal bones and cartilages. In the latter site they constitute the scurvy "rosary". These subperiosteal collections may be extremely painful and may closely simulate osteomyelitis of the limb.

Any injury is likely to be followed by a hæmatoma. Local œdema, often first noted round the tendo achilles, is another important sign.

Bleedings from mucous surfaces may be serious by reason of the profound anæmia they may cause.

This fully-developed picture of classical scurvy is now rare. Lesser degrees of scurvy—the so-called latent or subclinical scurvy—are far commoner and very hard to diagnose. Gingivitis is probably the earliest sign but it must be emphasized that there are many causes of this other than scurvy; pyorrhœa and its attendant gingivitis are indeed extremely

common among native soldiers. Increasing weakness and malaise, pallor and anæmia, loss of weight, and vague "rheumatic" pains in the limbs, are some of a host of possible early symptoms

Diagnosis —Vitamin-C deficiency is diagnosed on the evidence of deficient vitamin-C intake, the clinical picture, and capillary-resistance tests Certain laboratory tests have been proposed but none are entirely reliable and free from objection. The so-called saturation test, which is most generally used, is often difficult of interpretation.

Differential Diagnosis.—Distinguish from beriberi, purpura from other causes, rheumatism, osteomyelitis, and periostitis. It may be extremely difficult, especially in Indian sepoys, to distinguish scorbutic gums from the gingivitis associated with pyorrhœa

Treatment.—The symptoms of frank scurvy and of latent or subclinical readily respond to adequate vitamin-C therapy.

It is immaterial whether the vitamin is given in its natural form or as synthetic ascorbic acid, the thing that matters is to give enough

In both mild and severe scurvy the basic diet should contain at least 100 mg of vitamin C daily For treatment of mild cases give a further 100 mg, either in foods like citrus fruits or as synthetic ascorbic acid For treatment of severe cases, give synthetic ascorbic acid, up to 500 mg daily.

Oral administration is usually satisfactory, but in extreme cases it may be necessary to give ascorbic acid intravenously Large doses should be continued until a satisfactory clinical response has been obtained If the patient fails to respond, it is necessary to seek out the reason either the symptoms and signs arise from some other cause, or an unrecognized complication is hindering response to treatment

Other treatment is usually unnecessary, but a mild, astringent mouth-wash may be given if the mouth lesions are severe

Vitamin D (Calciferol) —This vitamin is concerned in calcium and phosphorus metabolism Important sources of vitamin D are fatty fish and the livers of the cod and halibut Although a diet may be deficient in vitamin D, the effect of sunlight may allow the individual to synthesize his own supply Evidence of vitamin-D deficiency has not been noted among the armed forces during the 1939–45 war

Vitamin K —This vitamin which is found in green plants, is concerned in the mechanism of blood coagulation Deficiency of vitamin K is always brought about by failure of absorption it may lead to serious hæmorrhage During outbreaks of infective hepatitis, the occasional onset of a hæmorrhagic tendency was said to have been associated with a low vitamin K concentration and to have been checked by intramuscular injections (2 mg daily) of vitamin K

Nutritional Anæmia.—During the 1939–45 war, nutritional anæmia was relatively common among certain categories of Indian troops The anæmia might arise as a result of iron deficiency, this form is best called iron-deficiency anæmia, but it is also known as hypochromic anæmia and microcytic anæmia Or the anæmia might result from deficiency of the specific hæmopoietic principle or principles present in liver and in marmite.

This form is best called macrocytic anæmia; it is not invariably hyperchromic. If both deficiencies are factors in causation, the condition is called dimorphic anæmia.

Iron-deficiency (hypochromic, microcytic) anæmia, which was found in Mohammedans and Hindus alike, was usually associated with two factors: the first, a dietetic factor, usually of long standing, caused by poor feeding before enlistment; and the second, a non-dietetic factor such as chronic blood loss from ancylostomiasis, chronic malaria, chronic dysentery, or something of this kind. The non-dietetic factor was often the more important. Macrocytic anæmia, often severe was noted especially among vegetarian Hindus.

Macrocytic anæmia of nutritional origin was also observed in a single group of white Dominion troops who lived for a time on a ration (not British) which consisted almost entirely of processed items and was low in calories, first-class protein, and vitamins of the B-complex. Similar anæmia was also seen among British and Dominion prisoners of war repatriated from Germany who had endured starvation conditions and forced marches for some months before their release.

Treatment.—In many cases, true nutritional anæmia is apparently caused by a combination of iron deficiency with lack of the specific hæmopoietic principle. Therefore iron along with some form of liver extract is usually necessary. Marmite or yeast in some form is often a useful adjuvant. Liver is best given by intramuscular injection as one of the less-refined extracts like hepalon in preference to one of the more-refined preparations.

Really severe degrees, especially of macrocytic nutritional anæmia, are usually very resistant to all forms of therapy; even an incomplete cure may require six months' to one year's treatment. In the severest degrees, that is if the red-cell count falls below two million per cubic millimetre, one or more transfusions of very carefully matched, fresh, whole blood are usually necessary.

The anæmia is only a symptom of such underlying conditions as poor feeding, ancylostomiasis, malaria, and chronic dysentery. These require discovery and appropriate treatment.

Famine œdema (kriegsodem, famine hypoproteinæmia).—Starvation or famine œdema is the outcome of two dietary deficiencies: low calorie value and lack of enough protein.

[illegible] German
[illegible] s
[illegible] d

undertaken long forced marches on inadequate German rations. A similar condition was common among recently-captured German (but not Italian) prisoners of war, who, before capture, had lived for long periods in the Western Desert on a poor diet consisting mostly of cereals. A high proportion of these prisoners also suffered from chronic dysentery

Diarrhœa, common in most nutritional disorders, is particularly com-
[illegible] 50 per cent of cases. It is
[illegible] ent's general
[illegible] to exclude a

specific cause such as amoebic or bacillary dysentery, or, if there is feve an enteric-group infection

Diagnosis.—There is a history—usually a recent one—of semi-starvation and this is often combined with an account of severe exertion. This history, along with the clinical picture, will clinch the diagnosis.

The patient may indeed present a striking picture: a pinched and usually pallid face, general emaciation, and thin arms, wrists, and hands, which are in marked contrast to the swollen feet, ankles, and lower legs. In severe cases there is generalized anasarca with marked œdema of the scrotum, ascites, and hydrothorax. Because the dropsy is gravitational and easily reversible, the face is seldom affected. The urine is often of low specific gravity but otherwise normal. Frequency and polyuria are common, especially when the œdema begins to subside as a result of improved diet. The liver and spleen are within normal limits, if anything they tend to be small on account of the chronic starvation.

The plasma proteins are low (usually under 5 per cent. instead of the normal 7 per cent.) and the normal albumin-globulin ratio is upset.

Treatment.—The aim of treatment is to improve the general nutrition of the patient as rapidly as possible and to replace the depleted plasma proteins by means of a diet containing a generous ration of proteins of high biological value.

It is important that the starving or semi-starved patient, with his greatly impaired digestive and absorptive functions, should not be overfed at the start, in this respect, indeed, he must be treated at the outset much as a newly-born baby is cared for. For the worst cases it has proved very effective to give skim-milk frequently by spoon—as in sprue. Janet Vaughan recommends dried skim-milk powder 60 g., glucose 40 g., water 500 c.cm.—the mixture to be diluted half-and-half at each feed with water, tea, or coffee. This may be given for three to four days, thereafter, fresh or dried eggs may be added.

Intravenous serum or plasma in 10 per cent. glucose solution may be given in extreme cases.

Protein hydrolysates (amigen, papain digest), which were favourab reported on in the Calcutta famine (1943), did not find the same favo in the treatment of the victims of the German concentration camps. Th question of their place in treatment is perhaps still open to further inquiry

PARATYPHOID FEVER

The paratyphoid fevers are world-wide in their distribution, and prevail wherever defective sanitary conditions favour their spread. Generally speaking, paratyphoid A infections are most common in the East, while paratyphoid B is more commonly met with in Europe and temperate climates generally. Paratyphoid C occurs in the Balkans, but a few cases are recorded annually from India, and many cases were seen in the Middle East during the 1939–45 war.

Etiology.—At least three separate and distinct bacilli are involved, *i.e.* *B. paratyphosus* A, *B. paratyphosus* B, and *B. paratyphosus* C. They

closely resemble *B. typhosus* in their morphology and general cultural characteristics, but differ from it in the way they behave with specific [illegible]

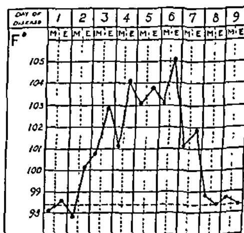
paratyphoid B have been traced to infected meat, but here there is a possible confusion with *B. ærtrycke.*

Thanks to the universal practice of chlorination, water infection does not seem to have bulked largely in the wars of 1914–18 or of 1939–45

Symptoms.—*Paratyphoid A and B*—The average incubation period is probably about ten days. It is not possible to discriminate clinically between paratyphoid A and B, which can be differentiated from one another and from true typhoid only by laboratory tests. The first runs a slightly longer course and seems to be on the whole a milder disease

The onset may be gradual like that seen in typical typhoid, but in the majority of cases it is comparatively sudden and in some it is exceedingly sharp. Headache and abdominal pain, or rather uneasiness, are the first signs as a rule, and in cases with slow onset there is general malaise, diarrhœa which may pass off, slight shivering fits, pain in the back and limbs, and sometimes epistaxis. The patient carries on till he is no longer fit for his duties. The opposite class of case is where a patient suddenly develops abdominal pain, which may be severe and colicky in type, diarrhœa and intense headache, feels feverish, shivers, may retch or vomit, and is speedily prostrated.

Fig. 45.



Short attack Paratyphoid   Gradual onset and rapid defervescence

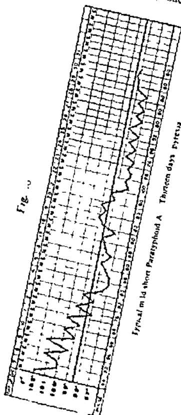
The onset is indeed very like that of influenza, but lacks the catarrhal element, though cough and sore-throat may develop later or may be present from the outset, or an early bronchitis may mask the primary infection. Vertigo and deafness sometimes occur, and a certain proportion of patients are constipated, especially in hot climates Pain over the region of the gall bladder has been noted in the earlier stages of the fever.

The temperature rises fairly rapidly, but to no great height—somewhere between 100° and 101° F

There would seem to be very slight cases of the disease where the patient is only really ill for about a week, but a typical paratyphoid B attack runs a course of anything between ten and eighteen days and a characteristic paratyphoid A exhibits a three weeks' pyrexia.

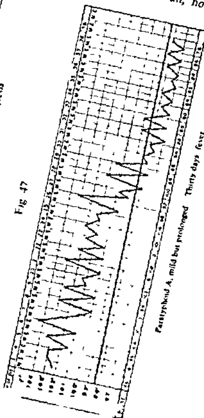
Even at the height of his illness the average paratyphoid case does not look seriously ill. The general temperature course is indicated in the accompanying charts (Figs 45 to 52), and only a small number of cases exhibit anything approaching a true typhoid state. In all, however,

Fig. [illegible]



Typical mild short Paratyphoid A Thirteen days pyrexia

Fig 47



Paratyphoid A, mild but prolonged Thirty days fever

especially in the early stages, there is a certain lethargy or apathy. A flushed face is rare and the eyes are dull and often kept about half closed owing to the headache, which is the patient's chief complaint.

The spiky nature of the temperature will be apparent and is very characteristic It rarely falls to 99° F. and as rarely rises to 103° F. In most cases it keeps swinging between a couple of degrees up at night and down in the morning, but occasionally missing the remission. Now and then one meets with a case showing intermission. In paratyphoid B

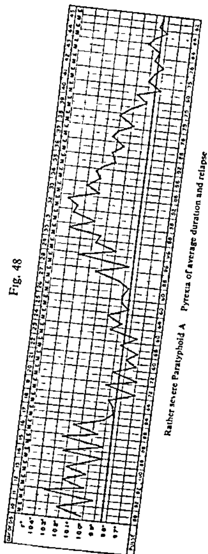


Fig. 48

Rather severe Paratyphoid A   Pyrexia of average duration and relapse

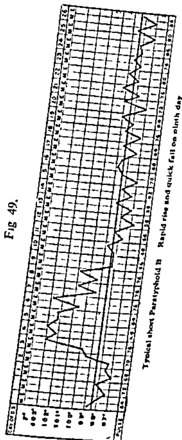
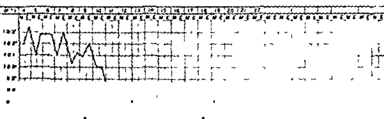


Fig 49.

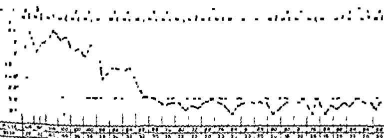
Typical short Paratyphoid B   Rapid rise and quick fall on ninth day

Fig. 50.



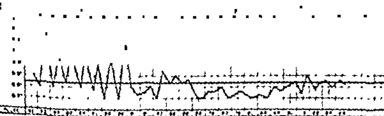
Typical rather severe Paratyphoid B   Eleven days' pyrexia

Fig. 51.



Severe toxic case of Paratyphoid B   Pyrexia of seventeen days

Fig. 52



Mild case of Paratyphoid B with intermittent temperature

infections so-called undulant cases have been described and a type with low irregular pyrexia. Of all symptoms the pulse rate is probably the most important for, unless the patient has been smoking, it is nearly *always slow and very often slower*, as compared with the temperature, than it would be in true typhoid. Thus, a pulse rate of 60 may coexist with a temperature of 100° or 101° F. It varies, however, and several have noted a high rate coinciding with a high temperature. Other notable features are a certain *compressibility* and *dicrotism* *Intense sweating* may occur, the patient being bathed in perspiration.

The tongue is dry and as a rule rather characteristically furred, there being a red tip, red edges, and central red channel with two separate patches of thick white or yellowish-white fur. In bad cases the regular dry, brown, furred, cracked tongue of typhoid is in evidence. There is little in the way of abdominal symptoms save a certain elasticity of the abdominal wall; the spleen is usually not palpable There may be tender-

Rose spots are very commonly seen. They come out in crops at intervals of three to seven days, probably as a rule between the seventh and tenth day, and last for three or four days. In a good many cases they are present only after the temperature has fallen to normal. When fully developed the spots are distinctly larger, redder, and more lenticular than those of true typhoid. Sometimes they remain of the typhoid type Their favourite sites are the lower ribs in front, the flanks and the back of the shoulders. When profuse they are scattered over the abdomen, and may be minutely vesicular or have an acne-like appearance In number they may vary from half-a-dozen to well over a hundred. It is said that in paratyphoid A infections the rash tends to be very profuse and may somewhat simulate that of measles. In paratyphoid B the rash is distinctly papular but markedly pleomorphic, the papules varying in appearance.

Some bronchial catarrh is often present, but severe bronchitis is not common.

It is to be noted that moderately severe cases often markedly *improve* a few days after admission to hospital, and this quite apart from any treat-

be associated with rigors. A case is on record where a relapse occurred thirty-nine days after the temperature had reached normal. There are slight and more severe forms. The latter are more or less recrudescences

Paratyphoid C.—Paratyphoid C differs from the other paratyphoid fevers in certain important respects. The causative organism is closely related to *B. suipestifer*, and at one time the two organisms were considered identical. Outbreaks of paratyphoid C develop most readily in a com-

munity already affected by some other disease, and in the past epidemics have been recorded in association with malaria and relapsing fever. During the 1942–43 epidemic of infective hepatitis in the Middle East, many cases of supposed infective hepatitis admitted to the special wards for that disease were proved by blood culture to be suffering from paratyphoid C. The infection is essentially a septicæmia without involvement either of the intestine or of the mesenteric glands. The causative organism can be isolated from the blood without difficulty, and seemingly at any stage of the disease. Fever may last from a few days to six weeks or thereabout, and the temperature curve is very variable in type—continuous, with marked remissions, or even intermittent. There is a peculiar liability to localized septic complications in the form of cold abscesses due to *B paratyphosus* C. Any part already weakened by trauma or by some other infection may be involved. Such abscesses have been recorded in the liver, gall-bladder, in joints, etc., and at the site of intramuscular injections of quinine.

During the 1939–45 war, paratyphoid kept cropping up in the Middle East in unexpected guises. In at least one case *B paratyphosus* C was grown in pure culture from a liver abscess confidently diagnosed on clinical grounds as amœbic, in another, the organism was isolated from an empyema secondary to a gun-shot wound of the chest.

Morbid Anatomy.—The following points are of interest:—

1. The lesions may be the same as in typhoid fever.
2. The large intestine is more commonly ulcerated than in typhoid fever.
3. The intestines may be acutely inflamed throughout their length, but the lymphatic tissue may escape.
4. There may be no change at all in the intestines. This is the rule in paratyphoid C

Prognosis.—This is good except in cases showing meteorism, severe bronchitis, certain other complications, or, and this is important, a persistently rapid pulse, *i.e.* above 100. At the same time it is well to remember that there are very severe and fatal forms of both types of infection.

Complications.—Jaundice may mask a paratyphoid infection, and should always be regarded with suspicion. A considerable number of complications are mentioned, the more important being hæmorrhage, perforation, and femoral thrombosis. The tendency for paratyphoid B infections to involve the large bowel and to be associated with abscess formation must not be forgotten. Paratyphoid bacilli (A and B) have been isolated from the stools of patients suffering from clinical dysentery with or without fever. Some of these may have been convalescent carriers. A case complicated by cerebral abscess has been recorded. Tachycardia may be troublesome during convalescence. Most of the complications met with in typhoid fever may also occur, but less commonly, in the paratyphoids. Perforation and the classical typhoid state are but rarely seen.

Diagnosis.—The bacteriological diagnosis is of great importance. Except in paratyphoid C, blood culture as a rule is positive only at the beginning of the disease. The value of the agglutination reaction in paratyphoid has been reduced to nothing in the Army by anti-typhoid inoculation, but this is a matter which cannot be considered here. A leucocyte count will show leucopenia. A long series of negative examinations of the stools must be made before paratyphoid infection can be excluded, and even then the bacillus may be missed. It is rarely found in the urine.

officers were more careful to view the stools of their cases this error would not so frequently occur. Other faulty diagnoses which have been noted are jaundice, influenza, bronchitis, rheumatism, tuberculosis, undulant fever, cholecystitis, and appendicitis. The condition is liable at its outset to be confused with phlebotomus and dengue fever and malaria by those unfamiliar with these diseases. *B. coli* septicæmia may simulate it, and can only be diagnosed definitely after bacteriological examination, while a so-called infective gastro-enteritis in which the whole dorsum of the tongue is furred, may closely resemble paratyphoid.

Prophylaxis.—This is essentially the same as for typhoid fever (p 321) and reference should be made to the section on this disease. In addition to T.A.B. vaccine special hygienic supervision of meat is required to lessen the risk of infection with *B. paratyphosus* B. This applies especially to all forms of pork, but it is probable that many outbreaks of food poisoning attributed to *B. paratyphosus* B in the past were really due to *B. ærtrycke*, which is indistinguishable except by detailed bacteriological analysis.

Treatment.—As for typhoid fever. Enemata are indicated in the earlier stages. Aspirin often relieves headache and hypnotics are sometimes required. Barbitone in two 5-grain doses in hot tea or as a tablet checks the profuse night sweat. Murphy's method of administering, drop by drop per rectum, a 6 per cent. cold solution of glucose has been highly recommended as an anti-thermic measure which has an excellent effect on the patient's general condition. Thirty to 40 drops are given a minute, and as much as 3 quarts may be administered in the twenty-four hours. A single injection occupies an hour to an hour-and-a-quarter. Liquid paraffin can safely be given in most cases to counteract constipation, but

especially acidulated drops, help to keep the mouth clean and promote the flow of saliva, thus diminishing the danger of suppurative parotitis. Fruit drops must on no account be given to semi-conscious or drowsy patients as they may be swallowed whole or inhaled.

It should be noted that many physicians now adopt, with apparent good

result and no increase of disasters, a far more generous diet than was formerly considered safe. In spite of this, great care must be exercised in the choice of diet during and for a few days after the febrile period.

PELLAGRA

Pellagra is characterized clinically by buccal lesions, gastro-intestinal disturbances including diarrhœa, nervous and psychical manifestations, and a symmetrical dermatitis affecting areas of skin exposed to sunlight or friction (Plate 24).

In the past, infections and toxic agencies were often put forward as the cause of pellagra, and such theories are still sometimes advanced. But since the early part of this century it has been accepted on almost conclusive evidence that pellagra is a nutritional-deficiency disease.

[illegible]

association with other diseases such as intestinal disturbances that aggravate the nutritional deficiency

Pellagra occurs among all races. In the countries where it is endemic, it is found chiefly in country districts and among those who lack the opportunity and resources to purchase protective foods such as meat and dairy products and whose principal article of diet is a cereal of relatively low nutritive value. Because pellagra was noted chiefly in maize-eating communities the early theory was that the disease was caused by the presence of a toxin in this cereal, but consumption of maize is not essential for the development of pellagra, and the disease occurs in communities whose staple article of diet is some other second-class cereal like polished rice.

Pellagra may occur at any age. It has been said that the fully-established disease is relatively uncommon among children, but careful examination of the children in pellagrous families often reveals early clinical signs of pellagra.

Etiology.—In the great majority of cases the clinical syndrome described under the name of pellagra is undoubtedly a multiple deficiency disease caused by a lack of more than one member of the vitamin-B-complex. But the discovery that nicotinic acid cured black tongue—a disease of dogs similar in its pathology to pellagra and common in localities where pellagra is endemic—and the application of this discovery to the human disease in 1937, when it was found that nicotinic acid cured the principal symptoms of pellagra, is enough to justify the present view that the essential features of pellagra are the clinical expression of nicotinic-acid deficiency.

Other members of the vitamin-B-complex known to be necessary to man (thiamin, riboflavin, and possibly pyridoxine or vitamin B_6) are

undoubtedly often deficient in the diet of pellagrins, and may contril to the symptoms. But the symptoms due to a deficiency of vitar other than nicotinic acid are to be regarded as complications of pell rather than essential features of the disease.

Nicotinic acid (Beta-pyridine carboxylic acid) in the form of its ar is combined in the body with phosphoric acid, the pentose sugar rit and the nucleotide adenine to form two co-enzymes: co-enzyme I cozymase, which has two molecules of phosphoric acid, and co-enz II, which has three molecules of phosphoric acid. Both co-enzymes widely distributed in animal tissues and both enter into the formatio essential enzyme systems used in transferring hydrogen in the oxidatio intermediary products of carbohydrate metabolism.

Although much is known of the action of these co-enzymes in metabolism, practically nothing is known about how a deficiency

function of the enzyme systems of which the co-enzymes form an inte part.

Pathology.—The pathological findings in pellagra are not specific, characteristic.

the body secretions pres nic cases, the inflammat rough and thick or thin atrophic, in either case there is increased pigmentation.

Microscopic examination shows that the skin lesions begin in the cor and show œdema of the papillæ, dilatation of their blood vessels,

undergo multiplication Vesicles form in the epidermis, and, become infected, the epidermis sloughs off, exposing the subjacent atrop corium. The deeper layers of the epidermis become pigmented eit

patches of pseudo-membrane and a stippled appearance due to presence of minute grey bodies; these, on histological examination, seen to be cystic crypts of Lieberkuhn. This appearance is said to nearly pathognomonic, occurring in only one other condition: spr In the later stages, there is atrophy of the mucosa of the colon, a superficial ulcers form.

Clinical Picture

1. *Early Manifestations*.—Although the fully-developed syndrome may seem to disclose itself suddenly, careful inquiry will reveal that it has been preceded by a long period of ill-health with symptoms, apparently trivial at first, advancing insidiously into the fully-developed disease.

The chief complaints during this prodromal period are, increasing weakness, lassitude, anorexia, dyspepsia accompanied by nausea, flatulence, and sensations of burning or discomfort in the epigastrium, and a tendency to diarrhœa. Mental symptoms appear, such as depression, irritability, and loss of power to concentrate. The early symptoms are not characteristic and may lead to a diagnosis of neurasthenia, unless the possibility of early pellagra is suggested by the association of these symptoms with one or other of the etiological factors usually concerned in pellagra. These include such things as a grossly-inadequate diet, the presence of factors increasing vitamin requirements such as pregnancy, infection, or hyperthyroidism, or the presence of a gastro-intestinal disease that interferes with absorption of vitamins.

2. *The Developed Syndrome*.—Here the clinical signs and symptoms fall into three main groups associated with the alimentary tract, the skin, and the central nervous system. They may be summed-up in the three words: diarrhœa, dermatitis, and dementia.

Alimentary Tract.—It is common for the digestive symptoms to precede the nervous symptoms, and for the skin lesions to appear some weeks or even months later.

In addition to the prodromal dyspeptic symptoms already mentioned the outstanding points relating to the digestive system are glossitis, stomatitis, and diarrhœa.

Pellagrous glossitis often first manifests itself as a hypersensitiveness of the tongue to hot or spiced foods, unaccompanied by any obvious signs. Later, along the margins and at the tip of the tongue, there is swelling and redness and indentations made by the teeth. As the disease progresses, the superficial epithelium desquamates, leaving a bright-scarlet, smooth, dry, beefy-looking tongue with atrophy of the papillæ and fissures of the surface. At this stage there is often secondary infection with Vincent's organisms or monilia; this produces a thick white coating which is ultimately shed. Aphthous ulcers of the tongue and buccal mucosa are common.

The inflammatory process extends to the buccal mucosa and the gums, and the stomatitis may be accompanied by increased salivation. The pharynx and œsophagus are involved, as well as the mouth, and this makes swallowing difficult or impossible.

The prodromal epigastric discomfort increases to a persistent burning pain; nausea and vomiting are frequent in the more severe cases.

The diarrhœa ranges in severity from a few loose stools a day to 15 or 20 motions containing blood and mucus. This severe diarrhœa is accompanied by tenesmus and there is often severe proctitis.

More than 50 per cent. of pellagrins have a histamine-fast achlorhydria.

Skin Lesions.—The dermatitis is perhaps the most characteristic

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and the nucleotide adenine to form two co-enzymes · co-enzyme I, or cozymase, which has two molecules of phosphoric acid, and co-enzyme [illegible]

Although much is known of the action of these co-enzymes in cell metabolism, practically nothing is known about how a deficiency of nicotinic acid brings about the functional and structural changes which characterize pellagra. At present all that can be said is that this deficiency of a component of the co-enzymes will presumably disturb the normal function of the enzyme systems of which the co-enzymes form an integral part.

Pathology.—The pathological findings in pellagra are not specific, but the lesions in the skin and colon are highly characteristic.

Skin that is exposed to light, friction, or the body secretions presents acute inflammatory lesions. But in chronic cases, the inflammatory lesions subside and leave the skin either rough and thick or thin and atrophic, in either case there is increased pigmentation.

Microscopic examination shows that the skin lesions begin in the corium and show œdema of the papillæ, dilatation of their blood vessels, and swelling of their endothelium; at the same time there is deterioration of the superficial fine collagen layer of the corium. Slight œdema of the deeper portions of the epidermis occurs and the cells of the basal layer undergo multiplication. Vesicles form in the epidermis, and, if these become infected, the epidermis sloughs off, exposing the subjacent atrophic corium. The deeper layers of the epidermis become pigmented either from increase in malanin or the formation of granules of an iron pigment. Old lesions show atrophy and reduction in the cells of the malpighian layer.

To the naked eye, the gastro-intestinal tract may either show little change, or the walls of the colon may be thickened and inflamed with patches of pseudo-membrane and a stippled appearance due to the presence of minute grey bodies; these, on histological examination, are seen to be cystic crypts of Lieberkuhn. This appearance is said to be nearly pathognomonic, occurring in only one other condition: sprue. In the later stages, there is atrophy of the mucosa of the colon, and superficial ulcers form.

In the nervous system there is degeneration of the axis cylinders of the pyramidal tracts and there are scattered areas of myelin degeneration in the ascending tracts of the spinal cord, chiefly in the posterior columns; the lesions resemble those of subacute combined degeneration. In the brain, the pyramidal cells show foci of chromatolysis; in late cases there is gliosis.

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More than 50 per cent. of pellagrins have a histamine-fast achlorhydria.

Skin Lesions.—The dermatitis is perhaps the most characteristic

symptom of pellagra, although it may be absent entirely. The acute lesions begin as a bright-red erythema, resembling sunburn, which is distributed over the exposed parts of the body or those subjected to the mechanical irritation of light clothing or to the action of the body secretions. The commonest sites are: the backs of the fingers and hands, the forearms, the dorsum of the feet and ankles in persons accustomed to go about barefoot, and the front of the neck, where the lesion forms the so-called "Casal's necklace". The lesions are almost always bilaterally symmetrical and are sharply demarcated from the adjacent healthy skin (*see* Plate 24). At this stage the skin is red and slightly swollen and it itches and burns.

In acute cases the lesion may progress to the formation of vesicles and bullæ, which crack with sero-sanguineous exudation and crusting. Some degree of secondary infection and ulceration are nearly always present.

The dermatitis most often appears in Spring; improvement usually occurs with the onset of cooler weather, when the skin dries and becomes brown rather than red; the surface desquamates leaving areas of pinkish, thickened skin with pigmented edges.

After repeated attacks and in chronic cases pigmentation is more general and the skin becomes scaly; over the legs and hands it may present a characteristic appearance in which irregular superficial cracks give it the so-called "crazy pavement" appearance. Hyperkeratosis with callus formation and pigmentation is characteristically seen in chronic cases, especially over skeletal pressure-points such as the knee, elbow, instep, and the front and back of the ankle; the appearance of these signs may indeed precede the dermatitis and the other manifestations of pellagra.

Nervous system.—Mental symptoms develop in anything up to one-third of the cases of pellagra. The milder mental disturbances are simply an intensification of the prodromal depression, irritability, and loss of power to concentrate. The patient enters upon a state of increased emotional tension: he is more excitable and sensitive than usual, he is often depressed and gloomy; and he is in a constant state of apprehension. Other features are loss of memory and deterioration in personality.

In the acute form of pellagra, these mental disturbances may progress to acute delirium; in progressive chronic cases, dementia is the terminal stage. In milder chronic cases, the mental disturbance may be the principal feature of the disease; it is accompanied by mild glossitis and diarrhœa and skin changes are minimal or absent. This is the so-called "pellagra sine pellagra".

Ataxia, spasticity, and loss of sphincter control—the results of the postero-lateral degeneration in the spinal cord—are seen in the more chronic cases. If sensory symptoms and changes in the tendon reflexes are present, they are most probably due to a complicating thiamin (B_1) deficiency.

Porphyrinuria.—Porphyrin is present in increased amount in the urine in many cases of pellagra, and some have attributed the light-sensitivity of the pellagrin's skin to a disturbance of porphyrin metabolism. But [illegible] and it does not appear

to be a diagnostic aid. The porphyrinuria is possibly related to the liver dysfunction that is nearly always present in pellagra.

Other Symptoms.—Other symptoms described in pellagra are probably complications that arise from a deficiency of essential nutrients other than nicotinic acid. The commonest of these are:—

(i) *Anæmia*.—Anæmia, usually macrocytic, is present in about half the cases of pellagra. The anæmia is probably due to associated deficiencies including the anti-pernicious anæmia factor, since it responds to the parenteral injection of purified liver extract.

(ii) *Signs of riboflavin (B_2) deficiency*.—The lesions of the lips (cheilosis and angular stomatitis), the scrotal dermatitis, and the butterfly-shaped area of seborrhœic dermatitis over the nose, naso-labial folds, and malar regions—all of which are commonly present in pellagra—are almost certainly due to an associated riboflavin deficiency. Some cases of apparently-nutritional dimness of vision without irreversible changes in the eye (*see* Nutritional Diseases) have been seen. They respond poorly to treatment with riboflavin or nicotinic acid. Apart from the eye changes, these cases have many features common to pellagra. Their nature is still a matter for investigation.

(iii) *Signs of thiamin (B_1) deficiency*.—In most pellagrins, the lesions of the skin and alimentary tract are accompanied by neuropathy which is marked by paræsthesiæ, hyperæsthesia or anæsthesia, pains in the calves, and alteration in the tendon reflexes. These manifestations are not relieved by nicotinic acid because they are the result of a complicating thiamin deficiency. They respond to administration of this vitamin.

(iv) *Signs of pyridoxine deficiency*.—It has been claimed that certain residual symptoms (great nervousness, irritability, insomnia, weakness, and difficulty in walking) persist in pellagrins treated only by the administration of synthetic preparations of thiamin, riboflavin, and nicotinic acid, but respond dramatically to the administration of 50 mg. of pure pyridoxine. It would be of interest to know the effect of this treatment on the cases with dimness of vision (*see* under (ii) above).

Diagnosis.—In the established case, the dermatitis, glossitis, and mental and gastro-intestinal symptoms present a characteristic picture and the diagnosis is easy.

In the early stages, and in cases without the characteristic dermatitis, the diagnosis is more difficult. A history of repeated attacks of the disease, particularly in the spring, and of dietary deficiency, either absolute or conditioned by some complicating factor, is of help in establishing the diagnosis.

Cases may simulate sprue if they are without dermatitis, and have glossitis, stomatitis, and gastro-intestinal symptoms as their predominant manifestations, analysis of the fæcal fat may help to distinguish the two conditions. Cases with glossitis, neuropathy, and macrocytic anæmia as

their presenting symptoms may be mistaken for pernicious anæmia with subacute combined degeneration of the spinal cord.

The dermatitis must be distinguished from conditions like "eczema" from exposure to the sun, occupational dermatitis, and erythema multiforme.

Unfortunately there are no reliable laboratory aids to the diagnosis of pellagra. The normal amounts of nicotinic acid and its derivatives in blood and urine, and their variations in disease, are not yet sufficiently established to make their determination of much diagnostic value.

Prognosis.—Most cases of pellagra develop in spring, become pro- ... Vague ... urrences ... becomes weaker and more emaciated. The outcome of untreated cases is death in about five years.

Acute cases have been described, especially in children, with death in the first attack because of severe gastric and nervous involvement.

Adequate treatment assures prompt recovery from pellagra, but relapse *is common, more often for economic than medical reasons,* since the pellagrin is usually driven back by economic necessity to his pellagra-producing diet once he leaves hospital.

Prophylaxis.—For the prevention of pellagra in normal individuals, *nothing more is needed than an ordinary good diet like that normally* ...

molasses, and fat pork that is so common among the poor in the southern ... of the United States ... but in ... Larger ... cereals, ... out half the nicotinic acid is derived from meat and fish

Because nicotinic acid is widely distributed among foodstuffs and is stable to heat and other processes of preserving and cooking, nicotinic-acid deficiency is unlikely except where the diet is grossly unbalanced. Nicotinic acid is readily soluble in water, but there will be significant loss from cooking only if the cooking-water and "drippings" from cooked meat are discarded.

Endemic pellagra is therefore an index of the inability of the affected population to secure a good, all-round diet rather than a measure of the concentration of nicotinic acid in any particular foodstuffs.

The optimum requirements of nicotinic acid in the adult have been placed at 15–20 milligrams a day. The minimal daily requirement to prevent pellagra *is thought to be in the region of 8–10 mg.*

Treatment.—In the vast majority of cases, nicotinic-acid administration

their presenting symptoms may be mistaken for pernicious anæmia with subacute combined degeneration of the spinal cord.

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Prognosis.—Most cases of pellagra develop in spring, become progressively more severe for two or three months, and then improve. Vague symptoms may persist or gradually disappear completely. Recurrences may develop every Spring, and with each attack the patient becomes weaker and more emaciated. The outcome of *untreated* cases is death in about five years.

Acute cases have been described, especially in children, with death in the first attack because of severe gastric and nervous involvement.

Adequate treatment assures prompt recovery from pellagra, but relapse is common, more often for economic than medical reasons, since the pellagrin is usually driven back by economic necessity to his pellagra-producing diet once he leaves hospital.

Prophylaxis.—For the prevention of pellagra in normal individuals, nothing more is needed than an *ordinary* good diet like that normally consumed by Western European or American peoples—in other words, a diet containing the usual amounts of meat, milk, eggs, wholemeal cereals, and fresh vegetables. Conversely, the diet must not consist mainly of highly-milled cereals, purified carbohydrate (syrup or sugar), and fat; in other words it must not *imitate* the pellagra-producing diet of maize, molasses, and fat pork that is so common among the poor in the southern part of the United States.

Nicotinic acid is widely distributed in plant and animal foods, but in most of them it is present *only* in relatively small amounts. Larger amounts are found in meat (especially the organs), fish, wholemeal cereals, and pulses. In the usual Western-European or American diet, about half the nicotinic acid is derived from meat and fish.

Because nicotinic acid is widely distributed among foodstuffs and is stable to heat and other processes of preserving and cooking, nicotinic-acid deficiency is unlikely except where the diet is grossly unbalanced. Nicotinic acid is readily soluble in water, but there will be significant loss from cooking only if the cooking-water and "drippings" from cooked meat are discarded.

Endemic pellagra is therefore an index of the inability of the affected population to secure a good, all-round diet rather than a measure of the concentration of nicotinic acid in any particular foodstuffs.

The optimum requirements of nicotinic acid in the adult have been placed at 15–20 milligrams a day. The minimal daily requirement to prevent pellagra is thought to be in the region of 8–10 mg.

Treatment.—In the vast majority of cases, nicotinic-acid administration

will promptly, even dramatically, relieve the acute symptoms. It will bring about progressive if slower return to normal of chronic lesions.

But the symptoms of pellagra are almost always the expression of a multiple nutritional deficiency, reliance should not, therefore, be placed on nicotinic acid alone As in all deficiency diseases, administration of the specific therapeutic agent should be accompanied by the institution of an adequate and complete dietary. When the effects of the primary deficiency have been relieved, cure should be completed and maintained by a proper intake of food In view of the multiple causation of the symptoms, it is of particular importance to use for treatment concentrates that are rich in nicotinic acid and also contain other accessory substances which are also probably deficient —for example, yeast or yeast extract

Nicotinic acid or its amide should be prescribed in amounts of from 200 to 500 mg daily in divided doses, the daily requirement depending on the severity of the case Nicotinic acid itself, if given in amounts exceeding normal tolerance (usually 50–100 mg by mouth) causes a pharmacological reaction flushing, burning, tingling, and redness of the skin, sometimes it may also cause headache, nausea, giddiness, and vomiting The effects do not last more than half-an-hour, but they are disturbing to the patient Nicotinamide, which is just as effective therapeutically as nicotinic acid, does not cause these unpleasant side effects, and is therefore to be preferred for treatment After sufficient improvement, usually within a week, the dose of nicotinamide can be reduced and gradually discontinued After about three months an adequate nutritious diet by itself is relied on to maintain the improvement

For very serious cases, or if nausea and vomiting prevent oral administration, nicotinamide may be given intravenously in 50 mg doses in sterile normal saline

As soon as possible, the patient should be given an adequate diet containing liberal amounts of milk, animal-protein foods (especially liver), eggs, fresh vegetables, and fruit Although milk has a low nicotinic-acid content, it is a very valuable food in the treatment of pellagra, possibly on account of its high riboflavin content A food-concentrate rich in vitamins of the B-complex—yeast, yeast extract (e g marmite), or Bemax —should be prescribed along with the diet

If there are well-marked symptoms of thiamin- and riboflavin-deficiency, t is essential to give preparations of these vitamins as well as nicotinamide n the early stages The dose of thiamin is 10 mg twice or even four mes daily, with an initial parenteral dose of 50 mg in severe cases, the ose of riboflavin is 5–15 mg daily

Dermatitis is the only symptom likely to require special treatment If condary infection of the skin has supervened, local treatment should be tituted with wet saline dressings and a protective covering, but antitic lotions should be limited to mild, non-irritating preparations

PHLEBOTOMUS FEVER

(Sandfly Fever)

This specific fever of short duration has a wide geographical distribution in Southern Europe, India, Africa, North and South America, and elsewhere. The infective agent is an ultramicroscopic virus which is intro-

The Vector.—The proven vector is *Phlebotomus papatasii*, but it is probable that other species are capable of conveying infection. It is a small hairy midge (Fig. 16). As *Phlebotomus* passes the winter in its larval stage, the fever is a disease of the summer months.

Whittingham and Rook have demonstrated that phlebotomus fever may be propagated by *P. papatasii* bred in a non-endemic area, infection apparently having been acquired from the parent flies.

The breeding-places of the fly are the interior of rubble and stone walls, crevices of caves and dug-outs, cracks and fissures in artificial embankments such as the earthen parapets of trenches, walls of old cellars, among heaps of damp stones, bricks, and tiles, and also in the surface soil. In all cases slightly moist organic matter is essential for breeding, and associated with this material there must be some crack or fissure providing the necessary protection, darkness, and moisture.

The adult flies shelter in similar situations, in clods of earth, beds of streams, and holes in trees It is worthy of note that they may be carried in timber and other cargo from place to place by sea-going vessels, a matter of some importance in districts where hospital huts, cooking sheds,

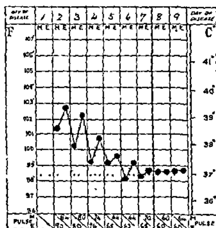
through thin socks or light cotton and linen clothing. A single fly may make many punctures and becomes sluggish after several suctions. One fly can infect.

At sunrise they vanish, either retiring to their breeding haunts or seeking dark corners in rooms or dug-outs. They dislike sunlight, but are attracted by lamps and candles. It is probable that they rarely traverse more than fifty yards or so and they do not fly high The bites are painful and, when numerous, the bitten part may be badly swollen Vesicles may form resembling those of chickenpox An attack by many flies effectively prevents sleep

The Fever.—It is short and sharp Incubation period two to seven days. Attack usually sudden, commencing with a feeling of chilliness and malaise. There may be rigors, never so severe as those of malaria Vertigo, very severe frontal headache, pain at the back of the eyes, accentuated by pressure on the globes and the least movement of the head, pains in the back and legs like those of influenza, and general stiffness of the muscles soon prostrate the patient, who becomes drowsy,

irritable if roused, but suffers from insomnia The face is very flushed and may look swollen. This flushing may persist long after the fever is gone. The conjunctivæ are injected so that the appearance resembles that sometimes seen in mastiffs or bloodhounds, hence the original name of "dog disease". There is no lachrymation or catarrh as is commonly present in influenza Anorexia with pain or discomfort in the pit of the stomach is a feature and constipation is the rule, though diarrhœa sometimes occurs, as does vomiting The tongue, clean at the tip and edges, is coated elsewhere by a thin white or brown fur. The fauces and palate are often congested and may exhibit small vesicles for which it is always well to look. Castellani describes small hyperæmic, roundish spots on the palatal mucosa Epistaxis is not infrequent at a late stage of the illness The skin is generally dry and even harsh, but may be moist. Apart from the face flush, which may involve the neck and upper part of the chest, there are no rashes, but these may be simulated by the numerous bites of the sandflies which, possibly as the result of scratching and irritation, may assume the appearance of a severe lesion, even simulating the exanthem of chickenpox. Typical temperature records are shown The rise is rapid By the evening of the first day's fever a temperature of 101° to 103° is reached It remains elevated for about twenty-four hours and then begins to fall, descending gradually on the third and fourth days and thus terminating very differently from the crisis of an ague fit (Figs 53 to 55) An after-rise of temperature is by no means uncommon in some outbreaks, but is usually slight and much less marked than that of dengue In one series observed in the Middle East during the 1939–45 war, 20 per cent of patients had a secondary rise of temperature after they had been afebrile for two to four days, in 11 per cent. there was a definite relapse from a week to three months after the original

Fig. 53



Type of Temperature in Phlebotomus Fever

Fig. 54.

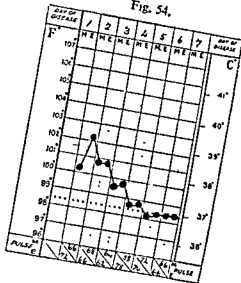
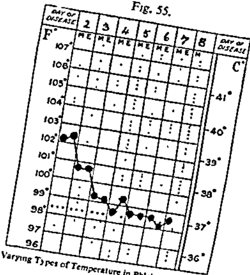


Fig. 55.



Varying Types of Temperature in Phlebotomus Fever

attack, a few had three attacks within three months The pulse rate throughout is comparatively slow and the blood picture is typical, *i.e.* a leucopenia with a relative decrease in the polymorphs. The eosinophiles diminish during the fever, but increase after it.

The patient may get better rapidly, or convalescence may be protracted and characterized by mental depression, lethargy, dyspepsia, and insomnia, the sense of taste and smell may be lost for a time. Recovery appears to

be the invariable rule Thus, during the 1939–45 war, mortality was nil among nearly 25,000 cases admitted to hospitals in the Middle East. The blood is infectious only during the first forty-eight hours of the illness and the infected sandfly becomes capable of transmitting infection only after the lapse of six days.

Differential Diagnosis.—A disease which closely simulates this fever is paratyphoid, especially in its early stages and milder forms, but abortive enteric, dengue, malaria, undulant fever, typhus, heat-stroke, and influenza may be mistaken for it In dengue rashes are present in 70 per cent of the patients, in typhus there is usually a leucocytosis, in influenza respiratory catarrh is a marked feature

In some outbreaks, in which a majority have been prolonged or unusually severe attacks, it has been difficult to decide whether sandfly fever or dengue was the cause of the illness

A small number of persons suffering from clinical sandfly fever have been found to have an increased cell-count in the C S F —up to 500 cells per c cm , only a minority of these showed other evidence (stiff neck, Kernig's sign, etc) of meningeal irritation The increased cell-count has usually been transitory, the fluid returning to normal within a few days.

In Malta (1943) one small group suffered from an illness, which, at the beginning was clinically indistinguishable from typical sandfly fever. Some 10 to 15 days later it was followed by acute attacks of epididymo-orchitis and in a few the sequel was atrophy of a testicle It is interesting to note that orchitis is sometimes mentioned as a complication of phlebotomus fever

Prevention and Treatment—Although phlebotomus fever is among the mildest of febrile illnesses it often occurs in explosive outbreaks, for this reason its prevention is of some military importance.

It should be remembered that newcomers to tropical or semi-tropical countries in which sandfly fever is endemic are more susceptible to the disease than others Consequently, in selecting units for operations in a sandfly-fever area during the sandfly season, men should if possible be chosen who have been "salted" by a residence of two or three years in the endemic area

Large numbers of susceptible persons drafted to certain localized areas where infected sandflies abound may be almost simultaneously attacked and have to take to their beds, all within a few days of one another, a unit may thus be suddenly put out of action for a time Hospital staff, especially those who take over new sites where there is much rubble and other builders' debris lying about, are specially prone to attack. Thus, 86 per cent of the staff of one general hospital went sick within a very short time from this cause The unit had recently removed to a new site on a sandy plain in Syria where there was much rubble and other debris close to the newly-erected stone buildings. Needless to say the routine of this unit was seriously dislocated for a time

As an example of the localized spread of the disease it is interesting to note that, whereas a high proportion of the orderlies suffered typical attacks, very few of the serjeants or officers fell victims, although only a

short distance separated their tented lines. Similar localization was noted in another hospital where a large proportion of the cases came from one part of the hospital compound—a small corner protected from both the sun and the prevailing wind.

During an explosive outbreak in a hospital it was noted that the occupants of wards on the first floor were just as prone to attack as those on the ground floor, although it is generally reported that sandflies do not readily enter rooms raised above the ground level.

Control of sandflies has been revolutionized by the introduction of D.D.T., and virtually complete area-control should be achieved around barracks, hospitals, and the like by combined indoor and outdoor spraying. (For full details, *see* Arthropod Pests—Midges, and Appendix I—Sandflies.) Dimethyl phthallate is an effective repellant of the greatest value in active service. Sandfly nets have been replaced by D.D.T.-

exposed to the wind

Treatment is entirely symptomatic.

Quinine is useless and may aggravate the symptoms. Aspirin and the salicylates in fairly large doses often afford comfort. Severe myalgia is benefited by the application of hot sandbags.

PLAGUE

Plague is endemic in parts of India, China, Africa, and elsewhere. *Epidemics are of common occurrence, and sporadic cases of the disease may crop up anywhere, especially among persons coming in contact with natives, and in the neighbourhood of docks.*

... and other

effective vectors.

The freedom from plague of parts of India has been attributed to the predominance of *X. astia* on the rats in such districts. Under similar conditions this species appears to be a less efficient vector of plague than *X. cheopis*, and Hirst has shown that it bites man reluctantly at temperatures over 80° F. As *X. astia* is a hot weather flea, some consider that ... meteorological conditions which are un-

as an acute or chronic ...

colour distinctions as both *R. norvegicus* and *R. rattus* may be brown. *Shortly before an epidemic, the disease appears as an epizootic*—first in *R. norvegicus*, the usual sewer rat. From this rat, infection is transmitted to *R. rattus*, the usual domestic rat, which, because of its close association with human dwellings, is responsible for carrying the infection to man.

Animals other than rats may serve as *reservoirs of infection, and in*

outbreaks of so-called sylvatic plague in Africa the various small mamm[als]
responsible were incriminated only after considerable research.

It is worth noting that the domestic animals, in times of epidemic, m[ay] suffer from pneumonic plague and become sources of infection. Virule[nt] plague bacilli were isolated from the lungs of donkeys in North Manchuri[a] and camels have been known to infect man.

It is now recognized that certain forms of merchandise, especially grai[n] and to a lesser extent raw cotton, because of the transported rats and fleas, are more to be dreaded as vehicles of plague infection than the human being *per se*.

There is some evidence to show that bed-bugs may be operative in spreading bubonic plague, but their role is certainly a minor one. Living plague bacilli have been found in human lice (*Pediculus humanus*), and it is thought possible that infection may be conveyed as a result of the habit of certain tribes of crunching lice between their teeth and swallowing them.

Pneumonic plague is transmitted from the sick to the healthy by droplets of sputum expelled in coughing, and also apparently by the invisible spray which pneumonia patients discharge from the mouth. There is some evidence to show that, in the case of primary septicæmic plague, infection may take place through the gastro-intestinal tract.

There are thus three recognized forms of plague and of infection.

The bacilli swallowed by the flea in feeding on infective blood multiply at its proventriculus, and the bacillary mass eventually extends into the œsophagus, thus blocking the entrance of the stomach. The starved flea makes violent efforts to get more blood, and the œsophageal contents regurgitate, thereby infecting through the skin lesion the healthy person on whom the flea is trying to feed. The flea itself does not necessarily die from the obstruction, but it is apt to do so if the weather is dry, presumably from lack of fluid. In this connexion it is interesting to note that plague does not maintain itself in epidemic form when the temperature rises above 80° F accompanied by a saturation deficiency of over 0.30 of an inch (Brooks).

Infection may also occur from the bacillus-containing fæces of the flea voided on the skin and rubbed into the wound.

When rats become ill or die, the fleas leave them and attack man. This is specially true when the epizootic has spread to *R. rattus*. Certain rat fleas may remain infective for at least six weeks.

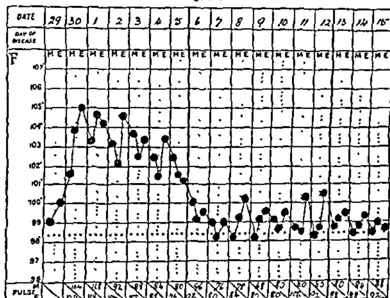
Symptoms.—The incubation period is from two to eight days. Rarely it may be extended to fifteen days, but a quarantine of ten days is usually considered sufficient. Prodromata are rare.

There is an ambulatory form, or pestis minor, in which the fever and prostration are slight. There may be some swelling and tenderness of the lymphatic glands, and there is usually at the site of the flea-bite the primary vesicle or pustule. It is very important to search for this and have it examined bacteriologically. Patients with pestis minor may suddenly collapse. They are dangerous, for they act as carrier cases.

All three forms of pestis major present certain symptoms in common, *i.e.* sudden onset, sharp fever, vertigo, great prostration, a drunken gait, appearance, and speech, and great cardiac weakness.

Bubonic Plague.—The patient suffers from headache and drowsiness and his face is pale and anxious. His features become drawn and haggard, his eyes bloodshot, sunken, and staring, and his expression often one of fear or horror. If still able to walk, he drags himself along like one in a maze or staggers about like a drunken person. As the fever increases his face gets hot, flushed, and bloated and his pupils dilate. The fever curve, as seen by the chart (Fig 56), is irregular and *the pulse is rapid and weak.* Thirst is intense, the furred tongue becoming dry and brown and sordes accumulating about the teeth, lips and nostrils. Delirium, and even convulsions, may ensue. The spleen and liver are enlarged, the urine *scanty but seldom definitely albuminous.*

Fig. 56.



Bubonic plague. (After Simpson)

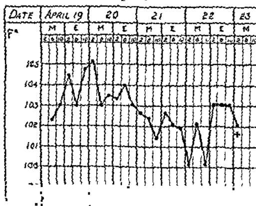
About the second or third day the characteristic bubo or buboes develop. The bubo is most commonly inguinal, as the word indicates, but the axillary, submaxillary, cervical, or other glands may be involved. As a *rule there is only one* bubo, which varies from about the size of a walnut to that of a goose's egg. The œdema of the surrounding tissue makes … [illegible] mall, hard buboes … [illegible] earance of buboes … [illegible] "White buboes", … [illegible] on other than the swelling, are of grave omen. Pain varies but may be very severe, sometimes it is complained of before there is any external evidence of the bubo.

In cases that are going to recover, improvement sets in about the [illegible]

and the patient convalescent.

Epidemics vary in their symptoms. In some, hæmorrhages, which may be petechiæ or large purpuric spots ("tokens") or definite bleedings from the nose, stomach, intestines, etc., occur, in others, gangrenous areas of skin form over and about the buboes or elsewhere ("carbuncles"), in others, pulmonary congestion and inflammation are present. In a small proportion of cases, plague blains may be a marked feature. These are

Fig 57.



Pneumonic plague (After Simpson)

superficial blebs, white or dark in colour, and swarming with bacilli. Carbuncles and blains usually indicate a heavy infection. Tokens invariably presage death—Shakespeare's "tokened pestilence where death is sure."

When a case ends fatally death usually takes place between the third and fifth days.

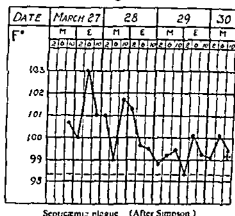
Pneumonic Plague.—Rigors and vomiting often characterize the onset. Cough, dyspnœa, and cyanosis occur, accompanied by a profuse, watery, blood-tinged sputum, which is quite unlike the rusty, tenacious sputum of ordinary lobar pneumonia. This plague sputum teems with bacilli and is exceedingly dangerous. The patient never has a chance. Moist râles are heard over the bases of the lungs, the toxæmia is intense, the breathing rapid, and death speedily ensues. The type of temperature is shown in the chart (Fig. 57). *It is important to note that a case of plague with*

pneumonia is not necessarily one of pneumonic plague, although there is grave danger that this dreaded form will supervene. Nor is the patient necessarily suffering from pneumonic plague simply because his sputum shows a few plague bacilli from time to time, this may happen in cases of bubonic plague that recover. In true pneumonic plague, at least in the later stages, the sputum teems with plague bacilli.

Septicæmic Plague (Fig. 58)—In the primary form the patient is at once rendered prostrate. His pulse speedily becomes thready or imper- [illegible]

have been cases where intense headache and fever were the only signs and where the patients died within forty-eight hours.

Fig 58.



Septicæmic plague (After Simpson)

Complications.—Pneumonia, toxic degeneration of the heart muscle, prolonged suppuration of buboes, iritis, corneal ulcers, and, in rare instances, blindness.

Morbid Anatomy.—All that need be mentioned here is the marked involvement of the lymphatic system with hæmorrhagic necrosis of lymphatic glands and the destructive action of the plague toxin on the endothelial lining of blood-vessels and lymphatics.

Differential Diagnosis.—The disease most like plague in its early stages is typhus fever. In both there is the same mental dullness and drunken aspect, but the course of the illness and the bacteriological examination soon clear up the difficulty. A venereal bubo may be mistaken for a plague bubo, a fulminant case of enteric for early bubonic plague, and an influenzal pneumonia for pneumonic plague

An ordinary septicæmia, some varieties of relapsing fever and a pernicious type of malaria may simulate septicæmic plague. It is worthy of

note that mixed cases of plague and relapsing fever are not uncommon.

Difficulty may arise from severe reactions in attendants and others who have received anti-plague serum after being in contact with a case of plague. These reactions, which may come on a few days after the injection, are characterized by high fever and generalized adenitis. It may be very hard to distinguish this serum adenitis, which is usually polyglandular, from that due to plague, which is usually limited to one or two glands, usually the inguinal glands. If there is any doubt, gland puncture should always be done and the juice examined for plague bacilli. If the cause of the adenitis remains uncertain it is wise to treat the case as presumably one of plague. In this matter, great care should be taken not to convey one's doubts and suspicions to the patient.

Prophylaxis—Personal.—Inoculation with Haffkine's or Kolle's vaccines affords some protection for a few months and is recommended in face of an outbreak. Haffkine's vaccine is usually given in a single subcutaneous injection of 4.0 c cm., and this is liable to cause an immediate febrile reaction, and occasionally a delayed reaction with lymphadenitis ten days later. Kolle's vaccine is given in two doses, of 2,000 million and 4,000 million, at ten-day intervals.

Living "avirulent" plague vaccines have been used on a large scale in Madagascar, Dakar, and the Netherlands East Indies. They are effective but are not yet free from risk.

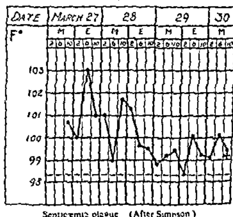
So far as bubonic plague is concerned, prophylaxis largely consists in warding off the attacks of fleas and bed-bugs. For measures against both, see section on Arthropod Pests and Appendix I on D.D.T. Fleas dislike the smell of iodoform, but so do most people, and the free use of iodoform powder would probably lead to undesired isolation.

Attendants on plague patients should wear leather or rubber gloves and overalls, and be protected about the feet and ankles by means of puttees or gum-boots. No food or drink should be partaken of in plague wards, and hand disinfection is essential. For a case of the pneumonic type, in addition to the foregoing measures, both patients and attendants should wear masks impregnated with disinfectant. All attendants should immediately be given 20 c cm. of anti-plague serum and should at the same time be injected with plague vaccine. The dose of anti-plague serum rather often provokes violent reactions, both immediate and delayed. Immediate reactions may include urticaria, marked swelling of the face, lips, eyelids, and tongue, hoarse voice from œdema in the neighbourhood of the vocal cords, and miscellaneous other signs. Delayed reactions, which may appear from the sixth day onwards, are usually severe enough to force the patient to bed. They include fever, headache, angio-neurotic œdema, widespread adenitis—the glands being discrete and painful, severe muscle pains, and so forth—temporarily disabling, but it must be remembered that they are non-lethal, last for only a week to ten days at the most, and are a small price to pay for the relatively high immunity against plague—notoriously a highly-fatal disease. The immunity from the serum is, of course, a passive immunity of short duration. Active, and more-prolonged immunity

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Septicæmic Plague (Fig. 58).—In the primary form the patient is at once rendered prostrate. His pulse speedily becomes thready or imperceptible at the wrist, he is pale and apathetic, and his temperature, owing to the magnitude of the infection, may scarcely rise at all. Hæmorrhages often occur and stupor, coma, or delirium herald speedy death. There have been cases where intense headache and fever were the only signs and where the patients died within forty-eight hours.

Fig. 58.



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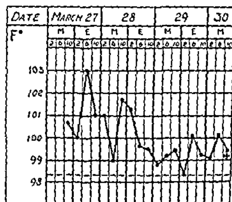
So far as bubonic plague is concerned, prophylaxis largely consists in warding off the attacks of fleas and bed-bugs. For measures against both, *see* section on Arthropod Pests and Appendix I on D.D.T. Fleas dislike the smell of iodoform, but so do most people, and the free use of iodoform powder would probably lead to undesired isolation

Attendants on plague patients should wear leather or rubber gloves and overalls, and be protected about the feet and ankles by means of puttees or gum-boots. No food or drink should be partaken of in plague wards, and hand disinfection is essential. For a case of the pneumonic type, in addition to the foregoing measures, both patients and attendants should wear masks impregnated with disinfectant. All attendants should immediately be given 20 c.cm of anti-plague serum and should at the same time be injected with plague vaccine. The dose of anti-plague serum rather often provokes violent reactions, both immediate and delayed. Immediate reactions may include urticaria, marked swelling of the face, lips, eyelids, and tongue, hoarse voice from œdema in the neighbourhood of the vocal cords, and miscellaneous other signs. Delayed reactions, which may appear from the sixth day onwards, are usually severe enough to force the patient to bed. They include fever, headache, angio-neurotic œdema, widespread adenitis—the glands being discrete and painful, severe muscle pains, and so forth. These serum-reactions are unpleasant and temporarily disabling, but it must be remembered that they are non-lethal, last for only a week to ten days at the most, and are a small price to pay for the relatively high immunity against plague—notoriously a highly-fatal disease. The immunity from the serum is, of course, a passive immunity of short duration. Active, and more-prolonged immunity

pneumonia is not necessarily one of pneumonic plague, although there is grave danger that this dreaded form will supervene. Nor is the patient necessarily suffering from pneumonic plague simply because his sputum shows a few plague bacilli from time to time; this may happen in cases of bubonic plague that recover. In true pneumonic plague, at least in the later stages, the sputum teems with plague bacilli.

Septicæmic Plague (Fig. 58).—In the primary form the patient is at once rendered prostrate. His pulse speedily becomes thready or imperceptible at the wrist, he is pale and apathetic, and his temperature, owing to the magnitude of the infection, may scarcely rise at all. Hæmorrhages often occur and stupor, coma, or delirium herald speedy death. There have been cases where intense headache and fever were the only signs and where the patients died within forty-eight hours.

Fig. 58.



Septicæmic plague. (After Simpson.)

Complications.—Pneumonia, toxic degeneration of the heart muscle, prolonged suppuration of buboes, iritis, corneal ulcers, and, in rare instances, blindness.

Morbid Anatomy.—All that need be mentioned here is the marked involvement of the lymphatic system with hæmorrhagic necrosis of lymphatic glands and the destructive action of the plague toxin on the endothelial lining of blood-vessels and lymphatics.

[illegible] early stages [illegible]

[illegible] soon clear up the difficulty. A venereal bubo may be mistaken for [illegible] [illegible]plague, and an [illegible] and a pernicious type of malaria may simulate septicæmic plague. It is worthy of

following proportions —1 oz. NaCN, 1½ oz. commercial H_2SO_4, 2 oz. of water,* but for use on a large scale, special apparatus is required.

cent. slaked lime.

Both the above when powdered and exposed to air form hydrocyanic acid gas.

Rat guards must be fixed on mooring hawsers and cables, but have only a limited value. A good rat-catcher on board ship is much more useful.

As regards pneumonic plague the freest ventilation is necessary, for it is in close atmospheres saturated with moisture that infection most readily takes place

Treatment.—Intensive sulphonamide therapy is of proven value in the treatment of plague. Sulphadiazine and sulphathiazole have so far given the best results, they must be given early in the disease and in sufficient dosage to produce their full effect. Sulphadiazine is the drug of choice The initial dose for the case of average severity is 4 0 g (60 grains) by mouth, followed by 1·5–2 0 g every four hours, day and night, until the temperature has dropped to normal. A maintenance dose is recommended of 0 5 g four-to-eight-hourly for a further 10 to 15 days.

In severe and late cases there is urgent need for parenteral therapy The initial dose advised is 0 1 g of sodium sulphadiazine intravenously [illegible]

so far been inconclusive

Chemotherapy has now largely replaced serum therapy in the treatment of plague

The symptomatic treatment must not be neglected and is that for any severe febrile condition with certain special indications, such as the application of cold and of ichthyol ointment or belladonna and glycerine to the buboes, their careful incision once suppuration is established and their careful aseptic treatment

Morphine is the best hypnotic Cardiac stimulants are nearly always required.

Prognosis in plague is notoriously difficult, and the recovery of seemingly

results from use of plague vaccines; these are not followed by violent reactions.

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carbolic requires five minutes' contact to prevent the growth of *B pestis* in sputum. The best disinfectant for the sterilization of the hands and gloves in plague work is methylated spirit.

Prophylaxis—General.—The usual quarantine period is ten days. The bacilli can persist in the bodies of recovered patients for three weeks; hence, to be on the safe side, convalescents should be isolated for a month.

The question of the destruction or disinfection of possibly infected fomites, such as clothes, skins, rags, etc., is important, for under certain

to protect food supplies from their depredations.

Cats and dogs should be kept away from plague patients.

The great question of rat destruction cannot be considered here in detail, but, so far as the use of traps is concerned, mention may be made of the value of tomatoes as a bait for rats. Portions of tomato can also be treated with phosphorus paste or other poison. Scraps of fish are very attractive to rats. The essential thing is to have a properly-planned campaign, based on careful study and survey of the local rat population. Expert help is of value in drawing up the plans.

R. rattus in India is most attracted by whatever grain forms the staple food of the district, and this should be used for bait. In hot weather fresh green vegetables, particularly cucumber, are useful. Traps should be oiled just sufficiently to prevent rusting and should not be washed over-much, for cleanliness renders rats suspicious (White).

The use of baited birdlime spread on boards has in some places superseded that of traps, while extract of squills, of which one-tenth of a milligramme will kill a rat, and barium carbonate, have also been employed in rat warfare. White recommends the last should be used as follows: One pound of powdered native barium carbonate is mixed

concentration, but care must be exercised owing to its poisonous properties. The gas may be generated by the admixture of reagents in the

following proportions :—1 oz. NaCN, $1\frac{1}{2}$ oz commercial H_2SO_4, 2 oz. of water,* but for use on a large scale, special apparatus is required.

For the fumigation of rat burrows, etc., on land two calcium products are largely used. Of these, Calcid, is supplied in briquettes, each of 20 g. Each briquette contains calcium cyanide 88 5 per cent, pure lime 11 5 per cent. Cyanogen "A" dust contains 45 per cent. calcium cyanide, 55 per cent. slaked lime.

Both the above when powdered and exposed to air form hydrocyanic acid gas.

Rat guards must be fixed on mooring hawsers and cables, but have only a limited value. A good rat-catcher on board ship is much more useful.

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In severe and late cases there is urgent need for parenteral therapy The initial dose advised is 0 1 g of sodium sulphadiazine intravenously for every kilo (2·2 pounds) of body weight, the initial injection is followed by one-half of the initial dose repeated six-hourly Oral therapy should be resumed as soon as possible. Alkali therapy has been recommended as an adjuvant to sulphonamide treatment Results with penicillin have so far been inconclusive.

Chemotherapy has now largely replaced serum therapy in the treatment of plague

The symptomatic treatment must not be neglected and is that for any severe febrile condition with certain special indications, such as the application of cold and of ichthyol ointment or belladonna and glycerine to the buboes, their careful incision once suppuration is established and their careful aseptic treatment.

Morphine is the best hypnotic. Cardiac stimulants are nearly always required.

Prognosis in plague is notoriously difficult, and the recovery of seemingly

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* ... . .

hopeless cases is likely to be attributed to whatever treatment happened to be employed. Moreover, as in other infections, a run of favourable cases may be encountered and mislead the observer about the curative value of some medicament. For these reasons it is not uncommon to see some particular treatment vaunted as effective, usually on the evidence of a small number of cases Up to the present, with the notable exception of the sulphonamides, extended trials have failed to substantiate any of these claims. But this is an old experience in the history of plague. During the dreadful London epidemic of 1665 we find Boghurst writing with grim humour: "Mr. Garencières saith the Plague is the easiest disease in the world to cure, and soe said Mr. Stoakes the Apothecary . . . but hee is dead since."

RABIES

(Hydrophobia)

Rabies is a specific infective disease of the nervous system characterized by a long incubation period. The causative agent is a filterable virus, possessing all the general characteristics of that group.

Etiology.—The disease occurs naturally as an enzootic among members of the canine tribe The virus is present in the saliva of an infected animal, and man acquires infection in practically every case by being

disease can be eliminated. In the British Isles, for example, by rigid application of quarantine regulations and muzzling orders for dogs, the infection has been stamped out. The disease occurs in any climate, and there does not appear to be any seasonable variation in its incidence

Besides the canine tribe, certain other animals are natural vectors. In South Africa, meercats and genets are responsible for transmitting the disease, and in parts of South America and in certain islands of the West Indies, certain species of blood-lapping bats of the order *Desmodus* transmit an unusual type of rabies, the clinical picture of which is that of an

to infection, but it is from
ntly infected. It is of con-
d be capable of recognizing
e symptoms in the dog and
d, all animals are in great
measure affected alike.

The dog acquires infection from a rabid animal. When the virus is introduced into its body, and comes in contact with nerve tissue, it passes along the nerve trunks to the central nervous system where it develops.

Having developed, it passes back along the nerves and can be demonstrated in the secretion of certain glands in the body, notably the salivary glands. The saliva is infective for a period of approximately ten days before symptoms of the disease are manifest It is important to bear this in mind when dealing with the question of persons who have been in contact with an infected dog

The length of time the virus takes to travel from the site of the bite to the central nervous system depends upon several factors, the more important of which are the distance the bite is from the central nervous system and the size of the nerve trunk involved The incubation period, consequently, will vary considerably. The period will, for example, be much shorter for implantations about the face than for implantations about the leg

Once the symptoms have become apparent, however, the disease runs a short course, usually of not more than five days, and always terminates fatally This is also of importance to bear in mind, since, if a dog suspected of being rabid is isolated for a period of 14 days, and at the end of this period is alive, it is safe to assume it has not been suffering from rabies. This test may be applied when there are no facilities for laboratory diagnosis

Pathological Changes in the Infected Dog—*Naked-eye Appearances*— There are no naked-eye appearances pathognomonic of this disease, although a striking feature is the marked degree of emaciation presented by a dog that has died from the infection It is much greater in degree than can be accounted for by the inability of the animal to partake of food during the short course of the disease The distinctive change is confined to the brain and for this reason a general post-mortem examination is not strictly essential But it is often very helpful It allows exclusion of other causes of death and permits examination of the stomach contents These may be very revealing because rabid animals often display a perverted appetite for bits of stick, stones, and other objects not normally found in the stomach of a dog

The utmost care must be taken by the operator to guard himself and his assistants from infection. The hands, wrists and arms must be covered, goggles may be worn, and the head of the dog may be immersed in carbolic to destroy virus about the mouth

Microscopical Changes—The demonstration of Negri bodies is conclusive evidence of rabies, for in no other disease are these characteristic features found. Negri bodies are cytoplasmic inclusions, and are found in their most highly developed form and in greatest number inside the large pyramidal cells and their processes of the hippocampus major * For this reason the hippocampus major is regularly examined for the presence of these specific bodies It is of considerable importance, therefore, that every medical officer should know where this structure lies

and how to expose it.* Negri bodies may be found in any of the neurons of the nervous system, but rabies cannot be excluded in the laboratory unless the hippocampus major has been examined.

Symptoms in the Dog.—The symptoms in the dog, with certain exceptions, are similar to those that occur in man. *The course of the disease, from* the time when the symptoms commence, lasts not more than five days, and during this period there are three stages.

(1) *Premonitory Stage.*—The characteristics of this stage are: altered behaviour, the dog seeks secluded corners, ceases to be obedient or may show excess of affection; perverted appetite, this is one of the most characteristic features of the disease in all the lower animals. These early symptoms may not always be pronounced, and this makes it difficult to recognize the disease at this stage, especially if there is no suspicion of any infection.

(2) *Stage of Excitement.*—This stage is characterized by aggression, snapping, unprovoked biting, aimless wandering and alteration of the bark to one of a high-pitched tone. Later, there is a staggering and erratic mode of progression, panting and outpouring of unswallowed saliva from the mouth. This is the "mad dog" stage and lasts for one or two days.

(3) *Stage of Paralysis.*—If the stage of excitement is short, dumb rabies may supervene without the furious stage ever having been observed. The paresis commences in the hind extremities, particularly noticeable in the tail which hangs down in a lifeless manner. Later, the [illegible]

affect the whole body.

The Disease in Man.—*Incubation Period.*—The period of incubation is variable and depends upon a number of factors, but it can be stated *generally that the nearer the bite is to the brain* the shorter the incubation period. The figures usually given are as follows: For bites about the face, thirty days; the arm, forty days; the leg, sixty days. It must, however, be emphasized that these figures are subject to *wide variation*—from seventeen days to three months or longer.

Onset.—There may, in some cases, be a prodromal stage with slight rise of temperature, and during this period the patient may complain of slight headache and insomnia, but more frequently the *onset in man is sudden.*

Symptoms.—During the short course of the disease three stages may be distinguished. More often, however, these stages are ill-defined, the end paralytic phase *developing rapidly.*

* To expose the hippocampus major the brain is laid down vertex uppermost [illegible] in thin horizontal slices till [illegible]

(1) *Premonitory Stage*.—The site of the bite often becomes irritable with pains in its neighbourhood. Fear and anxiety are often prominent in those who are aware of the possibility of their condition. There is depression with a desire for solitude, intolerance of loud sounds and similar stimuli, and periods of irritability. The voice becomes husky and difficulty in swallowing develops. This stage may last one or two days and gradually merges into the next phase.

(2) *Stage of Excitement*.—This stage is characterized by marked irritability. The tendon reflexes are exaggerated, and if the patient is observed, an expression of terror can be seen on his face. The condition progresses to one of hyper-excitability. The mind is clear, however, and if the attention of the patient is fixed he can, for a short period, control himself. This sudden change is, on occasions, most dramatic, and must be seen to be appreciated. As the disease develops these periods of calm become progressively shorter and the patient merges into a state of extreme excitability with spasms evoked by any stimulus. These spasms affect the pharynx and larynx and respiratory muscles first, and ultimately the whole body. Pharyngeal spasms are specially liable to be brought about by any attempt to drink (hydrophobia). Even the sight or mention of water may be sufficient to bring about a most distressing paroxysm. As the muscles of respiration become affected, breathing becomes laboured and noisy and a condition of air hunger develops. Later paralysis affects the throat with consequent difficulty in swallowing. The saliva becomes copious and viscid. Maniacal attacks may occur, but man rarely attempts to bite. The duration of this phase is one to two days and it merges imperceptibly into the next stage.

(3) *Stage of Paralysis*.—The paralysis becomes general and spasms cease. Consciousness usually remains till the end, but the duration of this phase is not many hours.

Course of the Disease.—From the time when the symptoms become apparent the disease does not last longer than three to five days. No established case of rabies contracted from a dog has ever been known to recover. The regular order of events in man is that paralysis supervenes upon a state of excitement and death occurs either quietly or in the midst of a paroxysm.

Diagnosis and Differential Diagnosis.—Clinically there is little difficulty in diagnosing this disease. In the differential diagnosis the possibility of hysteria, tetanus, atropine poisoning, and Landry's paralysis must be borne in mind. The laboratory diagnosis rests on demonstrating Negri bodies in the brain.

Prophylaxis.—Wild dogs and jackals in the neighbourhood of military quarters should be destroyed. In most military stations and camps there is a strict peace-time limit, usually about 4 per cent., to the proportion of men allowed to keep a dog. In war time, keeping of pets should be discouraged as much as possible. All surplus and ownerless dogs should be destroyed. All sick dogs should be segregated and tied up until seen

by the veterinary officer, or for 14 days. Suspected animals should be observed and not killed; if they are killed care should be taken to prevent injury to the brain.

Treatment.—Treatment of rabies by vaccine therapy is not curative in the strict sense of the term, but preventive. Advantage is taken of the long incubation period, in which immunity can be effected, to abort the infection before it has had time to develop. But as immunity takes time to become established vaccine treatment should be commenced as soon as possible after the bite, and carried out whenever an individual has been bitten or contaminated with saliva, even though no wound has been inflicted.

Treatment comes under four headings: (i) Local; (ii) Vaccine prophylaxis, (iii) Serum prophylaxis; (iv) General.

(i) *Local.*—The wound should be washed thoroughly with soap and water and then cauterized. It is most important to reach every part of the wound and this is by no means an easy matter with deep bites. The cauterizing agents that may be employed are pure carbolic, concentrated nitric acid, silver nitrate, potassium permanganate, or the actual cautery. For deep bites a knitting needle or similar piece of metal heated to a dull red heat makes a good cautery. It must be emphasized that local treatment does not do away with the need for specific vaccine therapy. Experimentally, it has been shown that the virus does not remain localized for any length of time.

(ii) *Vaccine Prophylaxis.*—This consists of a course of injections of anti-rabic vaccine.

The virus as it is recovered from an animal that has contracted the disease in the natural way has a great range of infectivity. It is termed

fifteen to twenty days. As the virus is passaged by subdural inoculations from rabbit to rabbit, the incubation period becomes progressively shortened until there comes a time when the symptoms appear constantly

respects, the more important of which is that it is less

rabies gradually lost their virulence when dried in the

rabies. The cords he injected first were avirulent,

injections, virulent. In the treatment of human cases, he commenced with a cord that had been dried for fourteen days and gradually worked up to one that was only one day old. This treatment formed the starting point of a system of preventive treatment that has become of world-wide distribution. Pasteur's original method of inoculation is still used, but a number of other methods have been developed.

The vaccine used in India is prepared by the method suggested by Semple. It is a killed virus vaccine and consists of a carbolized suspension of brain tissue containing the fixed virus of rabies.

The dose of the vaccine administered varies according to the degree of risk attached to the bite. For this reason bites are classified according to their situation, severity and number.

The vaccine is administered by subcutaneous injection in the abdominal region. Another site preferred by many who have experienced more than one course is into the loose skin between the scapulæ. If the quantity to be given exceeds 5 c cm the injection may be made in two places.

(iii) *Anti-Rabic Serum Prophylaxis.*—The use of anti-rabic serum as an adjunct to the routine vaccine treatment is at present under trial. The results, so far, are encouraging. The dose given is 20 c cm of the serum administered subcutaneously on each of the first two days of treatment, that is, a total of 40 c cm in addition to the appropriate doses of vaccine.

(iv) *General Treatment.*—No drug has been found to have any effect on the course of the disease. To alleviate the symptoms the most useful drug is, perhaps, atropine because it reduces spasm, but any of the depressants may be used.

Complications following treatment with the Vaccine.—The local reaction which accompanies the milder degrees of treatment causes little inconvenience. But with the larger doses, there may be marked local reaction and considerable tenderness. Headache is a common complication and with patients suffering from chronic malaria the treatment may bring about a relapse of malaria. These complications are trifling, however, compared with the possibility of a neuroparalytic accident.

Neuroparalytic sequelæ are not altogether rare and sometimes are fatal. They take the form of an encephalo-myelitis and range in intensity from a local paresis accompanied by paræsthesia to a rapidly ascending paraplegia of the Landry type. All intermediate stages may be seen. The onset of the symptoms calculated from the first day of treatment is nearly always within thirty days, and the earliest appearance of the symptoms may be within seven days of the commencement of treatment. The etiology of this condition is imperfectly understood. On the whole the prognosis of these accidents is better than would appear likely at their onset. Thus, a patient whose first signs are almost complete paraplegia and loss of sphincter control, characteristic of severe transverse myelitis, may so far recover within the space of a year or less as to regain sphincter control and show little more than slight residual spasticity. Unfortunately some cases have died, or there has been severe residual disablement. The appalling nature and invariably-fatal outcome of rabies justifies the risks that must be faced from use of the vaccine.

Laboratory Diagnosis of Rabies in the Dog.—The laboratory diagnosis is dependent upon demonstrating Negri bodies in the brain. The demonstration of the [illegible]

apron, a pair of gloves, and also goggles, if available.

Method of Removing the Brain

1. With a hammer crack the skull bones through the intact skin
2. Reflect the skin, remove the broken skull bones, and expose the brain.
3. Incise the dura and divide the brain down the centre into two longitudinal halves.
4. Lift out each half of the brain separately after severing the nerves, and dispatch to the nearest military laboratory.

If the specimen is sent by post or rail, it must be preserved. The whole brain may be sent or the hippocampus major which forms the floor of the lateral ventricle.

Preservation of the Brain.—The fluids that may be used are methylated spirit or 10 per cent. formalin; the formalin is to be preferred. If an attempt is to be made at isolation of virus one of the two halves of the brain must be preserved in 50 per cent. glycerine.

If refrigerated transport is available, it is best of all to send the unopened, unpreserved head to the pathologist who is thus free to choose the methods of preservation best suited to his own technique. It is always wise to take an early opportunity of finding out the procedure for any given place since local conditions may dictate the use of one technique rather than another. In any circumstances the specimen should be wrapped in a layer of cotton wool and placed in a container of adequate size with a wide mouth and the lid sealed securely. The container should then be dispatched in a box with sawdust.

Prevention of Rabies in Animals.—Anti-rabic vaccine for animals is now available and gives protection for at least six months. It is advisable to have dogs inoculated whenever cases of rabies are known to have occurred in the neighbourhood. A similar course of treatment is given in the case of the dog as in man. If it is known, however, that a dog has been bitten by a rabid animal, it is better to run no risk and to have it destroyed. Human anti-rabic vaccine is not of value for protection of dogs.

RAT-BITE FEVER

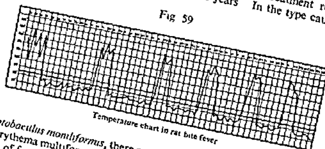
As a descriptive term, "rat-bite fever" leaves something to be desired. The rat is not the only animal whose bite may cause the disease; bites from cats and ferrets have also been incriminated. Moreover, there are two types of rat-bite fever caused by different organisms; *Spirillum minus* and *Streptobacillus (Haverhillia) moniliformis*. Nevertheless the term is

accepted usage, and, since both types of organism are ... this may help to maintain its use ... rat-bite fever ... perhaps ... than oth...

Sympt... ... usually in about 10 to 14 days (sometimes up to nine weeks) after the bite, there is an abrupt attack of shivering, malaise, and high fever, during the incubation period the local injury may have healed, but with the onset of symptoms it often becomes inflamed and tender with swelling of the related lymph glands.

In a day or two fever and other symptoms subside but in another three to ten days the remission is followed by a relapse. Purplish maculo-papular rashes are common, muscle-aches and joint-pains are often marked, the Wassermann is positive in about half the cases, and the spleen may become palpable. In the absence of treatment repeated relapses will continue for months or even years. In the type caused by

Fig 59



Temperature chart in rat bite fever

Streptobacillus moniliformis, there may be polyarthritis and a skin eruption like erythema multiforme. If the disease is prolonged the interval between bouts of fever may become shorter and shorter (Fig 59)

Diagnosis.—The diagnosis is not likely to be missed if the possibility of rat-bite fever is considered. Malaria and relapsing fever are excluded by repeated direct examination of stained blood films.

To confirm the diagnosis of rat-bite fever a blood culture should be made on Loeffler slopes plus 50 per cent serum-broth during a pyrexial period, 3 to 5 c cm. of blood should also be inoculated intraperitoneally into a suitable animal—guinea-pig, white rat, or mouse. Material aspirated from an enlarged gland may also be used. In about seven to 14 days after inoculation *Spirillum minus* may be demonstrated in films made from the blood or peritoneal exudate of the mouse. Dark-ground examination of the patient's blood will seldom reveal spirilla but will often mislead the inexperienced, who are not aware that various artefacts are readily mistaken for spiral organisms. *Streptobacillus moniliformis* will grow in blood culture in a medium with plenty of serum at 37° C in mice it gives rise to a general infection—often rapidly fatal—with localized lesions in bones and joints.

Bites from cats, rabbits, and dogs occasionally give rise to infection with *Pasteurella septica*. Acute swelling and pain quickly follow the bite

prostrated and often delirious. His tongue is moist but coated with a white or yellowish fur. It is to be noted that, in contrast to what is met with in typhus, the tongue continues moist throughout the illness save in very grave infections The patient is constipated, his skin is usually dry, and jaundice may appear, though it is often a mere conjunctival tinge Thirst, restlessness and vomiting, it may be of blood, complete the picture, but in a minority of cases there is an evanescent rash, either rose spots like those of typhoid or a reddish mottling. Hæmorrhagic forms of the disease sometimes occur. Liver and spleen enlarge. The urine is scanty and high-coloured. The appetite is poor, but occasionally a voracious hunger is developed.

The patient may pass into a toxæmic state with tympanites and hiccup and eventually die, but usually after five or six days of fever the first crisis takes place and is accompanied by profuse sweating and sometimes by diarrhœa The fall of temperature, often to subnormal, is both marked and sudden. There may be a descent of 10° F. in twenty-four hours. The change in the patient's condition is remarkable His appetite returns and after a day or two he may feel so well that he is keen to get out of bed. In debilitated patients, however, the fall of temperature may be accompanied by serious collapse. After a week or so of apyrexia the first relapse occurs Once again the temperature swings up and all the symptoms of the first stage are repeated, sometimes in a minor degree. Sweating, however, is usually more in evidence and the amount of urine increases.

The temperature remains elevated for three or four days and then a second crisis occurs. The patient may thereafter become convalescent or he may have a second and even a third or fourth relapse, but this is rare in the European form of relapsing fever.

In protracted cases convalescence is slow, but as a rule it is fairly rapid and recovery is complete.

Complications.—Jaundice, severe diarrhœa, epistaxis, hæmatemesis and hæmaturia, parotitis, herpes labialis, pneumonia, meningeal irritation, and ophthalmia may be mentioned.

Epidemics vary greatly in intensity. In time of war, among starved and debilitated communities, relapsing fever tends to be a serious disease, *and the mortality, usually slight, may be considerable.*

Diagnosis.—The spirochæte is found in the peripheral blood during the paroxysms, and can be stained by the Leishman or Giemsa stains, by carbol-fuchsin, or by alcoholic gentian violet. It is best demonstrated by the dark-field *method either in wet preparations* or dry stained films, but [illegible] can be detected in an ordinary cover-glass [illegible] d, and the film [illegible] preferably with [illegible] strength. The [illegible] seful. [illegible] ing the febrile periods.

Differential Diagnosis.—At the outset the disease may be mistaken for typhoid, typhus, trench fever, or cerebro-spinal fever, but the peculiar

course of the temperature is characteristic and the discovery of the parasite in the blood renders the diagnosis certain. [illegible] mention that an outbreak [illegible] fever [illegible]

[illegible] be mistaken for acute rheumatism. The pains of [illegible] and typhus, and of be confounded with malaria, and malarial attacks may follow relapsing fever and thereby simulate relapses. The disease is also apt to often seen during epidemics of the disease may be complicated by jaundice. On this account it may be confused with Weil's disease or, in endemic areas, with yellow fever

Prophylaxis.—The disease being louse-borne, this is the same as for typhus fever. Remember that the spirochæte has been found in the sweat and in the tears, and that it has been proved capable of passing through intact mucous membranes and the unbroken skin. A case is on record where the disease was acquired from infected blood accidentally squirted upon the face.

Measures for dealing with lice are detailed on p. 19 and in Appendix I.

Treatment.—Nursing, diet, and general hygienic measures as in typhus. After the crisis the patient is often ravenously hungry, and, if so, it is important to regulate his diet carefully, as injudicious feeding is apt to bring on bad diarrhœa and even dysenteric symptoms.

We now possess specifics in the arsphenamine series but the results of treatment are often disappointing. Neoarsphenamine is the most effective preparation and is given intravenously in doses of from 0.3 g. In the Egyptian form 0.6 g. doses have often been found necessary. One full dose as a rule suffices, but the drug should never be given if the duration of the attack indicates the crisis to be imminent, nor in any apyrexial period. If relapse occurs the injection should be repeated as the temperature rises. Sometimes an injection produces a temporary aggravation of the symptoms, but the curative action is usually rapid and certain. Albuminuria is not a contra-indication. Galyl has been found effective in doses of from 0.3 g. to 0.4 g., and other arsphenamine substitutes may be employed in corresponding doses. Sulphoxyl-salvarsan has been well reported on in doses of from 0.3 g. to 0.6 g. This last-mentioned preparation can be given intramuscularly.

In debilitated persons camphor, ammonia, digitalis and stimulants may be indicated. Sometimes the back- and limb-pains demand the use of opium. If hiccup is troublesome, blistering over the line of the vagus on the left side of the neck may be tried.

TICK-BORNE RELAPSING FEVER

Tick-borne relapsing fever is widely distributed throughout the Eastern and Western hemispheres. It is found mainly in three large areas:—

(1) Central Africa, including East and West Africa.

(2) Districts bordering on the Mediterranean, including the North

African Coast; Southern Spain; and an extensive area Eastwards to Persia, Turkey, and Transcaucasia.

(3) The greater part of Southern America, including many of the Southern States of the U.S.A.; Central America; and the Northern part of South America.

In Central Africa the disease was troublesome during both the 1914–18 and the 1939–45 wars. In this area the causative Spirochæte is named *S. duttoni*; it is morphologically indistinguishable from the other so-called species mentioned already. The chief vector of this spirochæte is the tick *Ornithdorous moubata* (Plate 2), one of the *Argasidæ*, concerning which details will be found in the section "Arthropod Pests". It suffices here to say that it bites at night; that it lives in huts, bandas, and rest- [illegible]

reaction. Infection takes place as a result of its infected fæces contaminating the tick-bite. One tick can infect.

The disease is usually sporadic or endemic; but it may assume epidemic *proportions if buildings where numbers of men sleep in transit become* heavily infested with *O. moubata*. The incubation period is difficult to determine, but probably lies between four and 18 days.

Clinical Picture.—Generally speaking, the clinical picture closely resembles that seen in the louse-borne disease.

The onset is sudden, with severe headache and fever. The rate of the pulse is quickened but not in proportion to the height of the temperature, which is usually 104° or 105° F. (Fig. 61). There is often an initial [illegible]

[illegible] absent. A minority [illegible]

palpable and it becomes increasingly hard and tender during febrile periods; the liver also is often enlarged. The total leucocyte count is normal or slightly raised. [illegible]

more than a rigor, headache, and 24 hours' fever. [illegible] rigidity, or both, may occasionally persist between the febrile bouts. The length of the afebrile intervals is remarkably constant in any particular case; there is no tendency for these intervals to lengthen as the disease continues. It is *true* that a febrile attack is often missed; but when this

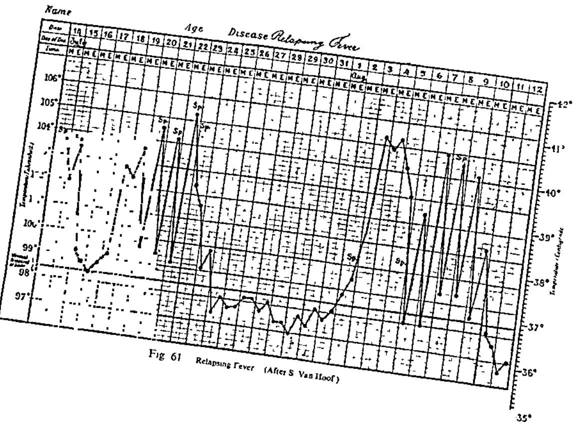


Fig 61 Relapsing Fever (After S Van Hoof)

happens the next bout of fever comes along after an afebrile period which is double the length that is usual for that particular patient.

Complications.—Among native troops in East Africa during the 1939–45 war, iritis was the commonest complication of relapsing fever, and in some outbreaks it affected 20 per cent. of patients. Iritis is never a *presenting symptom; it occurs during one of the relapses, and not during* the first febrile attack. It often continues for many weeks after the

treated by mydriasis with atropine. Any "red-eye" that develops during the course of relapsing fever should be regarded with grave suspicion and treated if there is any room for doubt.

Other complications are jaundice, lobar pneumonia, cerebral affections, and severe bronchitis, in native Africans they tend to occur in that order. Cerebral complications include coma, meningeal reactions, and focal

to

on

In Europeans, cerebral complications are more common, the commonest are meningeal reactions with lymphocytic pleocytosis or focal nervous damage, or both.

Severity.—The disease is a debilitating one, especially in Europeans.

illness.

The mortality in a recent large outbreak among native troops in East Africa was less than 1 per cent.

Diagnosis.—The diagnosis can be made with certainty only by finding the spirochæte in the blood. It is essential to take frequent blood films in all suspicious cases, and to continue doing so until the final fall of temperature indicates that the particular attack has ended. *Spirochætes* are seldom seen in the first film, but they become increasingly frequent in later slides. Sometimes they cannot be demonstrated at all. *It is worth* emphasizing the value of well-stained thick films, especially in the tick-borne *disease; for in this form spirochætes are normally much scantier*

laria, and, less

few subtertian

Prophylaxis.—This cannot be discussed here in detail. Because of the nature and habits of *O. moubata*, the disease is a "house" or "place" *disease, and in this respect is unlike louse-borne relapsing fever.* Native huts and rest houses should as far as possible be avoided. Infection is

favoured by sleeping on the ground or in wooden native bedsteads made with string or hide. Bandas should be properly constructed and tick-proof, there are many designs. Camps should be placed as far away as possible from native villages and buildings Periodical inspections of packs and blankets should be held, especially of newcomers Against ticks, D D T is of doubtful value—the question is meantime under study—but clothing impregnated with dimethyl—or dibutyl-phthallate gives a fair degree of protection Buildings in lines and camps which become infested present a serious problem Many devices have been tried to eliminate ticks or prevent their access Floors of huts have been cemented and experimental traps inserted in the walls But the tick has little difficulty in finding a hiding hole where it can lay itself up by day and wait for its nightly foray. Great hopes are held for the efficacy of some of the newer insecticides, but their realization on a large scale must await the future, at present the only efficient method of eradicating the ticks is to burn down the buildings and to fire the ground on which they stood.

In other parts of the world where tick-borne relapsing fevers are found, varying species of *Ornithodorous* act as vectors *O savignyi*, *O tolaje*, *O hermsi*, *O turicata*, *O tholozani*, and others. *O. turicata* and *O. tholozani* have been responsible for infections among those driven by war to live or take shelter in caves

The infecting organism is a spirochæte, apparently identical with *S recurrentis*, as mentioned above, it has been given a variety of names in the countries where it occurs. Tick-borne relapsing fevers differ from the louse-borne disease in that a number of small rodents (rats, squirrels, and so forth) and some larger animals (dogs, American monkeys) have been incriminated as reservoirs of infection. The vector ticks are found in the burrows of infected rodents In consequence, the infection in man is considered an accidental occurrence, and transmission from man to man is relatively rare

Treatment.—In treatment, skilful nursing is the keynote A single intravenous injection of neoarsphenamine,—0 45 g or 0 6 g at the beginning of each febrile bout—has been thought to be specific Recent experiments in East Africa do not support this view, and the drug is probably of little or no value, at least in the treatment of the disease as it is seen *in* that area. Animal experiments show that penicillin has some effect on the spirochæte, but the dosage that would be required for human treatment is so heavy as to be impracticable.

RICKETTSIAL INFECTIONS OF MAN

Rickettsiæ are minute diplococcal or rod-like bodies which can be demonstrated when suitably stained by Giemsa's fluid and examined microscopically Generally they are smaller than bacteria—less than 1μ in the longest diameter—but they exhibit considerable pleomorphism and larger and thicker forms or even chains may be seen

Characteristically the rickettsiæ infecting man cannot be cultivated on ordinary culture media and only develop in living tissue, in tissue cultures, or in the presence of fresh tissue Normally they develop in the alimentary

tract of certain blood-sucking arthropods. In the case of exanthematic typhus the rickettsiæ are taken into the louse with the blood feed, where they develop in the alimentary canal. Infective rickettsiæ not only pass out with the fæces, but also invade the intestinal epithelium and eventually cause the death of the insect. Other rickettsiæ appear to be harmless to their arthropod hosts.

When man or a susceptible animal is infected, either naturally or experimentally, with the fæces of arthropods containing certain types of rickettsiæ, the rickettsiæ invade and develop in the tissues, giving rise to various clinical conditions. Not all rickettsiæ, however, are infective to man.

Man is susceptible to a number of rickettsial infections, the most important of which are exanthematic or epidemic typhus, murine or endemic typhus, and Tsutsugamushi or scrub typhus of the Far East. The table below gives certain information regarding these diseases to which reference is made later.

Disease	Weil-Felix Reaction	Geographical Distribution	Insect Vectors	Possible Vertebrate Reservoirs
Exanthematic typhus	OX 19++++ OX K—	Europe, Abyssinia, North Africa, Belgian Congo, Asia Minor, Persia, North China, Mexico	Louse, *Pediculus humanus*	Man
Endemic or murine typhus	OX 19+++ OX K—	World-wide.	Rat flea, *Xenopsylla cheopis*	Rat (squirrel, shrew)
Tsutsugamushi disease (scrub or rural typhus of Far East and hill typhus of India)	OX 19— OX K+++	Japan, Formosa, Malaya, Java, Sumatra, New Guinea, India, Burma, etc	Larva of— *Trombicula akamushi* (Japan), *T deliensis* (Malaya), *T deliensis* (India), *T minor* (New Guinea)	Bandicoot, field mice, rat, shrew, and other rodents
Rocky Mountain spotted fever (Eastern and Western forms)	OX 19++ OX K++	U S A.	*Dermacentor andersoni*, *D variabilis*	Goats, hares and other small rodents
Fièvre boutonneuse	OK 19++ OX K++	Mediterranean Zone	Dogtick, *Rhipicephalus sanguineus*	Dog
[illegible]	[illegible]	[illegible]	Ticks, *Hæmophysalis* [illegible]	Dog?
[illegible] typhus	[illegible]	[illegible]	[illegible]	[illegible]
Q fever	OX 19— OX K—	Australia, U S.A	Ticks, *Hæmophysalis humerosa*, *Dermacentor andersoni*, *D occidentalis*, *Amblyomma americanum*, *Rhipicephalus sanguineus*?	Bandicoot
Trench fever	OX 19— OX K—	North Africa, many parts of Europe and Middle East	Louse, *P. humanus*	Man

Exanthematic Typhus

Exanthematic or epidemic typhus has been ...
since ...

vaccine greatly reduces the inci... ... crowd
severity for any who do not esca...
soldier the risk of death from t...

Etiology —It is ...
typhus in a cr...
of e...
M...
rheo...
path...
comp...
typhus are lic...
such patients...
in the early s...
murine char...
cycle they a...
becomes epi...
The infection ... ...species and the disease
the only
effective v...
lesions int...
or rubbed
powdered
mucous membranes of the upper respiratory passages ... suspended in the air and attacking the ...
The causal organism is a from of *Rickettsia* to which the name *R prowazeki* has been given

"Lice which have sucked blood contain...
producing ...
themselv...
feed, or ...
infective
producing ... placed upon the excoriated skin ...spectively are capable of duration of infectivity in the louse is unknown." (Nuttall) The

Pathology.—Exanthematic typhus is a disease of the smaller blood vessels The lesions are located chiefly in the endothelium lining the blood vessels of the skin, central nervous system, and skeletal muscles They may be demonstrated to a less extent in those of the viscera, heart, kidney, and testes. The reaction to the rickettsiæ is a degenerative change

giving rise to thrombosis. *There is also a proliferative reaction on the* part of the vascular endothelium giving rise to the characteristic microscopic nodules in the skin and central nervous system. It must be admitted, however, that autopsies on fatal cases sometimes show no characteristic lesions in the brain or elsewhere. Death from typhus is frequently the direct result of extensive proliferative reaction in the brain.

Incubation Period.—This varies between five and fourteen days, twelve days being the usual time.

Symptoms.—*These vary in different outbreaks*, and an attempt has been made to present a composite picture of the disease.

The onset may be slight, there being only the discomfort of a mild headache and pain in the back together with a loss of appetite; or it may be sudden and well marked, and the patient, in addition to the above symptoms, suffers from cold shivers, the eyeballs are tender on pressure and there is a sense of lassitude, malaise, and faintness. Occasionally general convulsions passing into delirium herald the attack. The period of onset lasts about two days (very occasionally it may extend to a week or more) and on the third day the symptoms become aggravated and the [illegible] appearance. The patient though [illegible]

excessive and the tumidity absent. The pulse rate increases while the temperature may still be normal—an important point in early diagnosis. Two other helpful early signs are bands of injection on the conjunctivæ, extending from either canthus to the cornea, and slight contraction of the pupil, a sign much stressed by the old physicians, at any rate in Ireland.

Epistaxis is frequent in some epidemics and may be profuse and persistent. There is a general reddening of the skin and what has been termed a "watercourse" appearance is not uncommon, red channels *running here and there and combining to form erythematous* patches. The conjunctivæ may become congested and some nasal obstruction, with slight discharge from the nose, may manifest itself. There is no splenomegaly at this stage.

On the second or third day the temperature begins to rise and after a morning remission runs up to 103° to 104°. Its usual course is shown in the charts, the fall being by lysis (Fig. 62). There may be preconvalescent rise.

Cases with remittent temperatures are encountered, and these are said *to do badly owing to cardiac trouble. The urine* is normal. The rash generally appears on the fifth day, being found first on the upper part of the abdomen and spreading thence to the chest and shoulders. The face *is so rarely affected that the complete absence of any rash on the* face is of considerable diagnostic value. The eruption often extends all over the body except the face, but it is more profuse on the trunk, *especially on* the back. The rash tends to be polymorphic and the individual lesions [illegible] group infections.
[illegible] xanthem is
[illegible] from rose

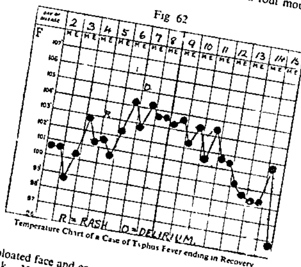
pink to purple or they may be so large as to amount to petechiæ or even purpuric patches The more hæmorrhagic rashes are seen in the severer cases, and patches of purpura are of specially evil prognostic significance Erythema and "marbling" sometimes occur but are often absent.

The macules retain their colour for five to ten days and are followed by brown staining for a period that varies from a few days up to six weeks. The latter period is more usual in cases of tick-borne typhus

Along with the rash there is a buccal erythema, and red spots may be seen on the palatal mucous membrane

As the rash develops the patient begins to look seriously ill The headache grows more intense, and he sinks into the typhus state, becoming dull and lethargic, with sluggish movements and a foul mouth What

Fig 62



Temperature Chart of a Case of Typhus Fever ending in Recovery

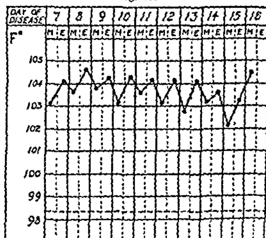
with his bloated face and congested skin and eyes, he looks as though he were drunk He is difficult to rouse, and lies on his back with a vacant stare (coma vigil) on his flushed face and, it may be, a tendency to squint, his voice is husky, his hands are tremulous, and he is somewhat deaf His cerebration is slow, he is very thirsty, he can scarcely show his dry, brown tongue Many classical descriptions have referred to a curious and characteristically pungent typhus smell resembling that from a cup-board of well-blacked boots This pungent aroma was doubtless common enough among the unwashed, dirty patients lying in the crowded wards, or less-than-wards, of our forefathers But it is less often perceived in these days of adequate spacing of beds and cleanly patients It is said to have been very marked in one large typhus camp in Persia but to have been strikingly absent among typhus cases in Belsen Camp, Germany

The breathing is rapid, and there is usually some bronchial catarrh with cough and thin expectoration. In the second week coma, low muttering

delirium, and retention of urine appear in all but the milder cases. At this stage the urine may contain albumin and casts, and the spleen will be found somewhat enlarged. The patient becomes more and more like a log. He is constipated, often wets the bed, and shows signs of cortical irritation such as twitching and hyperæsthesia.

If he is going to recover, a change for the better sets in about the fourteenth day; his mind clears, and within a week he is hungry and convalescent though weak and flabby. If he is going to die the coma deepens, his tongue continues dry and crusted, the temperature remains elevated or rises and the heart fails (Fig 63). Sometimes a patient will die after the crisis from exhaustion or complications There is some evidence to show that the virus remains in the body for three weeks after the fever abates.

Fig. 63.



Temperature Chart from the seventh day of a Case of Fatal Typhus Fever

case of

fulminant cases with early and violent delirium which succumb quickly, and what has been called the "high-tension type", with very severe headache and photophobia lasting throughout the entire pyrexial period, no delirium but mental irritability. The pulse is relatively slow but very full and bounding.

white counts

in so

severe

cases, there is a moderate, and occasionally a marked, polymorphonuclear leucocytosis during the second week of fever.

Complications.—Hypostatic congestion of the lungs, myocarditis, venous thrombosis, otitis media, parotitis, bed sores, gangrene of the

feet, and pemphigus may be mentioned Diarrhœa is sometimes so profuse as to require treatment The disease may be followed by peripheral neuritis and distressing neuralgias, but the convalescence is usually rapid and complete Internal-ear deafness and a confusional mental state may persist for a considerable time into convalescence

Prognosis.—The prognosis in the young adult who is reasonably well fed is very fair, but in those debilitated by famine and those over the age of forty years the outlook is uncertain. Those who develop early delirium are very apt to die

Diagnosis.—As an aid to diagnosis the production of artificial stasis of the vessels is said to be useful Where the rash is not characteristic or is sparingly developed place a bandage round the arm. The resulting engorgement of vessels shows up the exanthem more clearly, and the red maculæ can be observed to take on a blue, cyanotic hue, which eventually

[illegible]

group of fevers contain antibodies that react with certain strains of *Proteus* organisms

Weil-Felix Reaction.—The true nature of the reaction is still imperfectly understood, but although the sera of typhus patients may agglutinate a variety of *Proteus* strains, the so-called specificity of the reaction is

[illegible]

closely related to OX19 than to OXK, and for the sake of clarity the Weil-Felix reactions in different rickettsioses in the table have been limited to the strains OX19 and OXK As will be seen from this table the sera of patients suffering from exanthematic typhus agglutinate suspensions of Proteus OX19 only.

The agglutinins may be detected as early as the fourth day in certain cases of exanthematic typhus, but usually are not appreciable until a day

[illegible]

The sera of normal individuals may agglutinate suspensions of both OX19 and OXK in low dilutions, and such agglutination is more frequently observed with OXK suspensions. Any reaction with a serum diluted 1-100 or more, however, must be regarded as very suggestive. But the

most important criterion is the rapid rise of agglutinin titre as the disease develops.

The sera of individuals suffering from diseases other than typhus may agglutinate O suspensions of Proteus X. Chronic brucellosis, toxoplasma in adults, tularæmia, and typhoid fever in inoculated subjects are the chief examples. Although there may be early and appreciable titres with OX suspensions, it is very rare to find any significant rise in titre as these diseases develop.

Conversely the sera of patients suffering from typhus may agglutinate

titre with the particular *Proteus* suspension steadily increases, whilst the titres with the other antigens do not show any significant increase. It may be of interest to note that with *Bact. typhosum* suspensions early and appreciable titres with the H, O, and Vi antigens may be observed.

The Weil-Felix reaction is a valuable test but it cannot differentiate louse-borne (epidemic, exanthematic) typhus from flea-borne (murine) typhus. In the 1939–45 war, rickettsial agglutination tests with epidemic and murine rickettsiæ as antigens have been used in the Middle East and elsewhere. When the test is carried out under proper conditions with good suspensions, it can afford the greatest help in showing whether an outbreak is of the epidemic or the murine variety.

The differentiation is of epidemiological importance because a case of louse-borne typhus may initiate a serious epidemic, but there is little danger of a similar catastrophe from a case of the murine disease, which is primarily a disease of rodents, infection in man being accidental. Unfortunately, the test is a delicate one to handle. It demands an expert to prepare good, reliable suspensions, and a skilled worker with a keen sense of responsibility to set up the test and read it. van Rooyen, reporting on a large series of tests done in the Middle East, found that the louse-borne (epidemic) disease occurred almost exclusively during the winter and spring, and that murine typhus was prevalent during the summer months.

Differential Diagnosis.—Typhus has specially to be distinguished from typhoid and paratyphoid, while it may also be mistaken for lobar pneumonia, influenza, cerebro-spinal fever, measles, relapsing fever (may be also lice-borne), plague and septicæmia.

Treatment.—A satisfactory specific treatment has not yet been reported. Sulphonamides and penicillin are useful in the treatment of secondary

a good and conscientious nurse can do more for the typhus patient than all the medicines in the Pharmacopeia.

The apathetic or semi-conscious patient with severe typhus is very apt

to suffer from dehydration and salt depletion, both of which require constant attention. When enough fluid cannot be given by mouth, as often happens with a semi-conscious patient, parenteral administration of fluids is essential. Typhus patients lose weight and flesh rapidly and many suffer from obstinate anorexia, consequently every effort should be made to introduce sufficient nourishment, including a liberal supply of first-class protein in as palatable a form as possible. The aim is to give a fluid or semi-fluid diet of at least 2,400 calories with a minimum of 100 grammes of protein of high biological value and at least double the normal requirement of vitamins and mineral salts. Small, frequent feeds are best. Sleep rhythm may be reversed, with nocturnal insomnia and restlessness which is often extreme, this may require sedative treatment. Morphine should not be withheld from suitable cases.

Cyanosis is treated with oxygen, preferably administered through a BLB mask. The mouth, back, and bladder require special attention. By meticulous attention to hygiene of the mouth and to pressure points, every effort should be made to prevent suppurative parotitis and bed sores, both can be prevented by a keen and adequate nursing staff. Retention of urine with overflow is not uncommon, it is best dealt with by regular catheterization. Patients with typhus should be carefully watched for concurrent malaria and secondary infection, appropriate early treatment being given as required.

Prophylaxis.—The prevention of exanthematic typhus in any community where endemic typhus exists is dependent on the prevention of [illegible]

the hygiene organization.

D.D.T and anti-louse powders containing this most valuable agent (AL 63, Marks III and IV) have revolutionized the prophylaxis of all louse-borne infections including typhus. (*See* Arthropod Pests and Appendix I).

In dealing with any outbreak of exanthematic typhus, medical officers, nurses and hospital attendants are obviously exposed to greater risks than the rest of the community and in past epidemics this group of individuals has suffered greatly from the disease, yet they can be most ill-spared under such conditions. They must take several obvious precautions. In the first place, whoever is or is not immunized, medical, nursing, and hygiene personnel must be fully protected by vaccine (3 doses of 1.0 c.cm. at weekly intervals) and their inoculations must be kept up to [illegible]

appear in clouds when a lousy person is undressed.

Lousy clothing must be taken from an infected patient before his

admission to hospital; it must then be removed and sterilized by heat (*see* p. 16) and the patient must be thoroughly deloused. Thereafter he is not a source of danger to his attendants or others. The stretcher, blankets, and personal belongings must also have attention.

Contacts of cases must be sought out and deloused by dusting them with anti-louse powder (*see Arthropod Pests and Appendix I for details*). An efficient case-finding scheme is of the greatest importance and so is an efficient delousing organization prepared to deal with the great numbers that may require treatment in epidemic times. Contact between troops and the lousy population is reduced to a minimum and known infected areas are put out of bounds. Mass immunization of civilian populations requires large supplies of vaccine and it is seldom feasible; all troops should be fully protected with the best-accredited vaccine available. That now in use in the British army consists of a mixture of killed epidemic and murine rickettsiæ preserved in formalin, which causes momentary stinging on inoculation. The organisms are cultured on egg yolk, and, in those sensitized to egg, anaphylactic reactions may develop; adrenalin must, therefore, be at hand for immediate treatment of any such complication. Otherwise the vaccine causes little or no disturbance in a normal person.

Other Fevers belonging to the Typhus Group

Other members of the group are named in the first part of the table on p. 258. It will be seen that with the exception of murine typhus, which is world wide in its distribution, these conditions are restricted to certain territories and that generally their incidence is seasonal according to the insect vector. The table in question is by no means complete for there is little doubt that many fevers, now called P.U.O. in the absence of an exact diagnosis, in tropical and subtropical areas belong to this group of diseases.

The clinical picture and pathology of the group are essentially those of the principal member, exanthematic typhus, but generally the symptoms are less severe.

Rocky Mountain Spotted Fever, however, is usually a severe disease

hands and the soles of the feet.

SCRUB TYPHUS

(Tsutsugamushi disease, Japanese river fever, mite typhus, K-typhus)

Scrub typhus is widespread over many areas in South-East Asia and the South-West Pacific, being found in Ceylon, Burma, Malaya, the Dutch East Indies, New Guinea, Formosa, and Japan. Severe outbreaks have rred among troops operating in many of these countries.

act as reservoirs of infection. In Assam and Upper Burma the buff-breasted rat and Assamese tree shrew were found to be natural carriers. The rickettsiæ are transmitted from one generation to another by way of the egg.

Pathology.—Generalized intense congestion of the internal organs is the main post-mortem finding. Scattered sub-pleural hæmorrhages and patchy bronchopneumonia are common. The lymph glands are usually enlarged and the spleen is often about twice its normal size (i.e. just palpable). As in other forms of typhus the small blood vessels, especially of the lungs, heart, brain, and skin show local perivascular infiltration with monocytes, lymphocytes, and plasma cells.

Incubation Period.—Usually about 12 days. Extremes 8 to 18 days.

Symptomatology.—The onset is usually sudden with headache, fever, and shivering, this may be preceded by malaise for two or three days. The fever often swings violently during the first few days; thereafter it is usually of the sustained plateau type and may be anywhere between 101° F. and 105° F. As a rule it lasts from 12 to 16 days (extremes 7 to 28 days). Occasionally the pyrexia is irregular with drenching sweats. The fever usually terminates by lysis. Headache is almost invariable, and is usually very severe, in distribution it may be frontal, occipital, or generalized over the calvarium. Soreness and stiffness of the neck may cause suspicion of meningitis. The mental state is characteristically that of typhus. Drowsy apathy is the rule in moderate and severe cases, mental confusion is common, and deafness may give an appearance of greater indifference than is really present. In spite of the lethargy, nsomnia is common. In severe cases the apathy may be replaced by, r may alternate with, periods of restlessness and delirium during which the patient may leave his bed, and even the hospital, unless he is carefully watched. A bloated face with injected eyes is characteristic of severe cases, but of course this appearance may be seen in many other diseases.

In a proportion of cases varying from 6–75 per cent. a local bite or eschar in the shape of a shallow-punched-out ulcer may be seen if it is carefully sought for. Often it is on the trunk or thigh or on some area where clothing constricts. But it may be found anywhere. The eschar is usually scabbed over and resembles a small cigarette burn.

Some 95 per cent. of patients show generalized glandular enlargement. The glands are discrete, rubbery, and tender and appear between the third and fifth days of fever. They usually disappear after a few days.

The rash which appears on or about the fifth day in about 50 per cent. of fair-skinned individuals consists of a blotchy maculo-papular eruption usually confined to the trunk and proximal ends of the limbs. It is by no means always present and may be very hard to detect in dark-skinned persons.

Pulmonary symptoms appear in a great proportion of all but the mildest cases. These include hoarseness, unproductive cough, slowed respiration (which may be of central origin), and cyanosis. Diffuse bronchitis is the commonest objective sign, radiologically, universal mottling of both lung fields is a common finding.

Cardiac dilatation, which may be considerable, a rising pulse rate (to

120 or more), and low blood pressure (80/55 or lower) are evidence of grave cardio-vascular embarrassment.

In one-third of the cases, the spleen is palpable from about the tenth day.

Albuminuria and cylindruria are common. Oliguria and rising blood urea usually denote dehydration but may be due to renal involvement.

There is no characteristic blood picture. A polymorphonuclear leucocytosis, which is usually due to secondary infection, sometimes occurs during the second week.

The *complications*, which are usually due to secondary pyogenic infection, include various septic pulmonary lesions, of which bronchopneumonia is the most common, bullous impetigo, and suppurative parotitis. Less-common complications are axillary or inguinal bubo, venous thromboses, and optic atrophy.

An attack of typhus often activates latent malaria.

Many cases run a mild course throughout with a shortened febrile [illegible]

from a variety of septic complications and sequelæ.

Muscle-pains are usually complained of in the legs and shoulders during the first week out of bed.

Tachycardia with diminished exercise-tolerance, internal-ear deafness, visual disturbances such as diplopia and difficulty in focussing, and mental confusion may persist for three to four weeks.

Secondary fever that lasts for a few days or up to a week follows the primary attack in some 10 to 20 per cent. of cases.

Prognosis.—The mortality has varied from 2–25 per cent. in recent epidemics in the forces, the highest death-rate occurring among those exhausted from any cause such as chronic malaria or marching long distances on short rations. The majority of deaths have occurred in the third or fourth weeks of the disease. Bad prognostic signs are: fever lasting more than 18 days, pulse-rate exceeding 120, respiratory-rate of over 34, cyanosis, restless delirium, tremor of the hands, and plucking at the bedclothes. The heart symptoms may be very persistent, but permanent cardiac lesions are rare sequels. The important thing, in convalescence, is to prevent the development of a cardiac, or any other, neurosis.

[illegible]

the rash (it may not appear) on or about the fifth day or the development of a high enough titre in the Weil-Felix reaction, usually from the seventh to tenth day onwards (extremes: fifth–twentieth day). *Agglutination* [illegible]

against *Proteus OXK* suspensions; it either fails to agglutinate *Proteus OX19* and *OX2* or agglutinates them only to low titres in the same range as normal serum.

A rickettsial agglutination reaction like that used in the different diagnosis of epidemic and murine typhus has not yet been evolved.

Prevention.—The life history of the species of trombiculid larvæ whic act as vectors of scrub typhus is imperfectly known, but it appears probabl that the infected mite remains infective throughout its life and transmits the infection to its progeny. They are highly selective in their choice of locality, being very often found in the ground near water, especially in "scrub" and above all in ground that has once been developed and then allowed to revert to jungle—the so-called "secondary" jungle.

The larval mite usually approaches man by way of the feet and legs; thence it makes its way to the body and often feeds where its progress is held up by clothing tightly applied to the body, there the resulting eschar is usually found. Rats and small wild rodents, especially field-mice and shrews, probably form the reservoir of infection, clusters of larval mites may be found attached to these creatures, especially to their ears.

Three species of trombiculid mites, *T. akamushi*, *T. deliensis*, and *T minor* have been implicated in the spread of scrub typhus.

Man possesses little natural resistance to the disease and the attack-rate is therefore high. One attack conveys a high degree of immunity and this doubtless explains why the indigenous adult population suffers little from the disease in most areas—they have probably been infected early in life.

There is no cross-immunity with epidemic, murine, or other forms of typhus, this is not surprising because the serological reactions are notably different. A vaccine against scrub typhus has now been prepared by British workers from the lungs of infected cotton rats. Experimentally in animals it has given encouraging results and its mass-production for man was undertaken in time to launch a limited field trial before the Far-East war ended. The results are awaited. At all events the vaccine is not yet generally available, and freedom from the disease depends, therefore, entirely on general measures.

If possible, areas known or thought likely to be infested with trombiculid mites should be avoided as camp sites or resting places. Open areas of jungle covered with low scrub or grass and close to water are to be avoided, especially if they are "secondary" (reverted) jungle. If the tactical situation does not permit the avoidance of such localities the low scrub and grass over the whole area should be removed along with the top 5 inches of soil by a bulldozer. Scrub and long grass should *not* be cleared by hand in dangerous areas, nor is firing of the area recommended. f scrub must be cleared by hand, gauntlets should be employed for the ork. Immune natives should be employed if possible, but it is often fficult to get a reliable history of an earlier attack.

When men are working in mite-infested areas, shirt sleeves must be ...pt rolled down and trousers must be long with their ends tucked into socks. Gaiters or, preferably, puttees and boots should be worn at all times. Men should neither sleep nor rest in direct contact with the ground.

Dibutyl phthalate (D.B.P.) and dimethyl phthalate (D.M.P.) are efficient mite-killers, D.D.T. is not of value. D.B.P. is used in the

British Army because its effect lasts longer than D.M.P. Properly smeared into clothing it will greatly reduce mite biting and the incidence of mite-borne typhus. Two ounces of D.B P. a man a fortnight is enough to impregnate shirts, trousers, socks, and puttees—one ounce is rubbed into the clothing in use and the second ounce is applied to the spare clothing. Impregnation must be done by hand as a proper drill. How long the garments remain effective depends on the amount of hand-washing and heavy rain they must stand up to. The important thing is that a properly-impregnated garment immobilizes mites in five minutes and later kills them altogether. This greatly reduces the probability of their being able to reach and bite a part of the body. Benzyl benzoate promises to be perhaps even more effective.

The patient with scrub typhus need not be isolated when admitted to hospital since man-to-man infection does not occur. Special action regarding contacts is also unnecessary.

TRENCH FEVER

This condition, apparently a distinct and hitherto unrecognized disease, was first reported among the troops in France in the war of 1914–18, but occurred in the Salonika area and seemingly also in Egypt. There is evidence to show that it was introduced into the Mediterranean area from France. There is no record of its occurrence in East Africa, but it was reported from Mesopotamia (Iraq).

Trench fever apparently disappeared as a clinical entity soon after the 1914–18 war, but two localized institutional outbreaks of a similar fever, in both instances associated with lice infected by a member of the *Rickettsia* group of organisms (*R. weigl*), were reported from Poland, the last outbreak occurring in 1939. Whether this fever, known as Weigl's disease, was identical with trench fever is unknown. During the winter campaign of 1941–42 trench fever reappeared in the German Army on the Russian front. There it threw a considerable strain on the medical and army organization for cases were numerous and hard to recognize with cer-
[illegible] the intention of

Cultures of these rickettsiæ inoculated into volunteers have set up an infection clinically resembling trench fever. These rickettsiæ are not pathogenic to rhesus monkeys, mice, rats, rabbits, or guinea-pigs.

Etiology.—It is generally accepted that trench fever is due to *Rickettsia quintana*, found in the gut and excreta of infected lice. The louse, *P. humanus*, has definitely been proved to be the vector. The infection is usually derived from the excreta of infected lice scratched or rubbed into skin abrasions.

The fact that it is the excreta which are infective explains cases of trench fever occurring in wounded men who have not harboured lice for long periods, because the dried infected excreta blown on to a raw surface will

readily cause the disease A man may be entirely free from lice at the time he develops trench fever, the louse that infected him having left some time previously, or he may have contracted the disease from blankets, etc., contaminated with infective louse fæces.

It has been shown by Byam that the virus in louse fæces can resist drying at room temperature, exposure to sunlight, and hot water and soap as used in washing clothing by hand, and can withstand keeping for at least four months The virus is not affected by twenty minutes' exposure to dry heat at 80° C., but moist heat at 50° C. will sterilize it in twenty minutes. So that clothing, although effectively deloused, is not necessarily disinfected.

Lice become infective after a period varying from five to eight days from an infecting feed, and probably remain infective for the remainder of their life. They cannot transmit the virus through the egg to their offspring. Lice have been infected by feeding on a patient on the 443rd day of the disease (Byam).

Incubation Period.—The incubation period of the naturally occurring disease is difficult to estimate with accuracy, but experimental evidence suggests that it is in the region of eight days.

Symptoms.—In considering the symptomatology we are at once confronted with a difficulty, inasmuch as the term Trench Fever, an unsuitable one in any case, has been loosely applied to include not only the true trench fever, which is a definite relapsing fever, but also at least two other febrile conditions, commonly classed as P.U.O., one of an influenza-like type, the other recalling an enterica infection. It is not surprising that this error has been made because, apart from the pyrexia, the symptoms of these three diseases, as pointed out by the British Committee on Trench Fever, are indistinguishable from one another. As the Committee states, "All exhibit similar pains, all produce enlargement of the spleen, none show intestinal or renal symptoms of any importance, and all are apt to produce tachycardia".

Here only the true relapsing trench fever will be considered. Even then there is apt to be confusion, for there are two forms of fever which occur at different stages of the disease.

Briefly the symptomatology is as follows:—

Prodromal symptoms rare and unimportant Onset usually sudden, with headache, dizziness, pain chiefly in the legs and back. It may, however, be generalized, and abdominal pain is not infrequent. Pain behind the eyes, especially when they are moved, is a notable feature.

Attention is usually directed to the pain in the limbs, which is always worse at night It may be of a dull aching, gnawing or boring type, or be acute and lancinating, lasting for many hours. This latter form constitutes the now well-known shin pains, which are felt in the bone and have been attributed to neuralgia of the nerves in the periosteum. The general pains have been attributed to an infectious fibrositis. The pains may shift about, and very often begin about 5 or 6 o'clock in the evening. They may be associated with great superficial tenderness, so that not even the weight of the bedclothes can be borne. Sometimes at the start the weakness of the legs is so great that the patient cannot stand.

Alternate shivering and sweating is a peculiar and very constant feature, while some authors describe cases with vomiting and diarrhœa and a rare type presenting, at the onset, cerebro-spinal symptoms. The conjunctivæ are congested, the tongue is dry with a yellow fur down its centre flanked by red margins. There is usually constipation.

The spleen enlarges, and in 70 to 80 per cent. of the cases small erythematous spots or papules make their appearance chiefly on the chest, back and abdomen. They are usually flush with the skin and pink in colour,

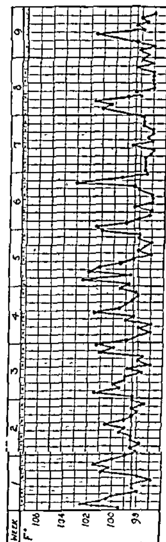


Fig. 64.

Trench Fever. (After Byam.)

and disappear on pressure There may be few or a couple of hundred, and they are often evanescent. Sweating is common, catarrhal symptoms rare, albumin in the urine not infrequent.

Labial herpes is often seen. The blood shows a leucocytosis and an increase of polymorphs up to 90 per cent. during the febrile periods. The lymphocytes are said to show a slow relative increase during convalescence.

In bad cases the patient becomes anæmic, and owing to lack of sleep—the result of the severe pains—he presents a worn, haggard look, and suffers from mental depression. As a rule, however, the eye remains clear and bright, thus differing from the dull and half-closed eye of the enterica group of fevers.

The pyrexia calls for special mention (Figs. 64 to 68) The two forms already mentioned as occurring at different stages of the disease are in order of sequence —

1. An irregular remittant and intermittent fever lasting for a period rarely exceeding four weeks. It may be so slight as to escape notice
2. A definitely intermittent fever, often showing a regular periodicity, and sometimes extending over a period of many weeks.

These two together constitute the complete pyrexial wave of the disease, but it is important to note that the first form, when well marked, may present three types of temperature curve.—

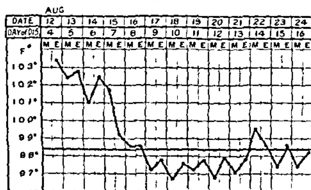
(*a*) A short, influenza-like fever wave, lasting about three days.

(*b*) A similar wave followed, usually on the sixth, seventh, and eighth days, by a febrile relapse, the interval being afebrile. Irregular fever may follow

(*c*) The initial wave may run more or less into the relapse and produce a so-called saddle-back (dengue-like) or pseudo-typhoid temperature *Irregular fever may follow.*

The above are the types recognized by the War Office Investigation Committee.

Fig. 65.



Trench Fever

Fig. 66.

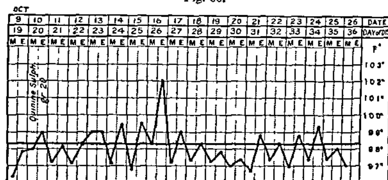


Fig. 67.

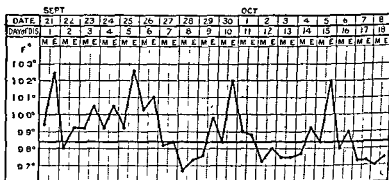
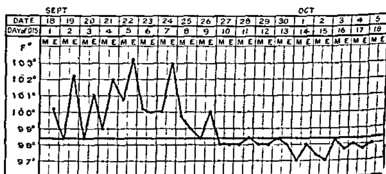


Fig. 68.



Figs 66-68 —Charts illustrating various types of Temperature in Trench Fever.

it may not appear for many months, the disease in the meantime being apparently in quiescence as, in such cases, the chances of reinfection were excluded.

This secondary fever may be merely a single "spike" or a series of "spikes", suggesting the appearances met with in relapsing fever.

The temperature shoots up to about 104° F. In the single "spike" form it falls rapidly and continues on or about the normal line. In the multiple "spike" form the fever recurs at intervals which usually vary in duration, but may be periodic (often four-day periods). The later "spikes" tend to be more irregularly spaced. In the non-febrile periods the temperature is subnormal. The highest temperature is usually reached in the evening, but this is not invariably the case.

While the above appears to be the general course of the disease, it is clear that many irregularities occur. Indeed at least four irregular clinical types have been described, but into these we need not enter.

The pulse-rate in the early stages is quickened, corresponding to the rise of temperature, later it tends to be slow in relation to the degree of fever.

A loss of sensation, varying in degree, has been noted in the middle and later stages of the disease.

Trench fever, though not a fatal malady, is a very crippling one, for it not infrequently leaves behind it a train of unpleasant sequelæ. Of these the most important is disordered action of the heart, or irritable heart, the result of a myocarditis which may produce dilatation or merely a muffling of the first sound. On the other hand, the first sound may be loud with a slapping impulse.

Tachycardia is common, and there is dyspnœa on exertion. Other troubles are anæmia and persistent pain, especially in the shins.

Diagnosis.—Unlike the majority of the other rickettsial diseases of man the blood-sera of patients suffering from trench fever do not contain antibodies that react with the O-antigens of *Proteus* X strains. Some regard the condition of the tongue as very characteristic, while the "spiking" of the secondary fever is highly suggestive, as are also the "shin pains". As a matter of fact, the clinical picture has to be studied as a whole and other diseases excluded by careful laboratory tests.

Differential Diagnosis.—Influenza, malaria, enterica, dengue, phlebotomus fever, relapsing fever, undulant fever, and the milder forms of leptospirosis may be mentioned as the diseases most likely to be mistaken for trench fever.

Prophylaxis.—This consists chiefly in measures directed against lice. (*See* Section on Arthropod Pests and Appendix I.) The urine and sputum must be disinfected, as they contain the infective agent.

Treatment.—For the most part this is symptomatic. Aspirin, 20 grains at night, seems to be the best analgesic. Phenacetin and opium are useful.

Mustard leaves ease the pains in the shins, as do hot belladonna stupes. When these and other pains are very severe lumbar puncture gives relief, but vinum colchici should first be tried, as it has been found helpful. Some employ Collargol, 10 c.cm. of a 1 per cent. solution intravenously, the injections being repeated at two or three-day intervals. Collargol has been proclaimed a specific cure in acute cases, but substantiation is lacking.

Rest, blood tonics, regulated exercise, and thyroid therapy are indicated for the subsequent debilitated condition.

SCHISTOSOMIASIS

Schistosomiasis in various degrees of severity is widespread in Africa, where both *Schistosoma hæmatobium** and *S. mansoni* are represented.

be due to *S. mansoni* only. *S. japonicum* causes the variety of the disease found in the Far East, the symptomatology of which appears below.

Etiology.—The schistosomes constitute a family of sexually-differentiated trematodes. Of the nine known species, two, *Schistosoma hæmatobium* and *S. mansoni*, seemingly occur as a natural infection in man only. *S. japonicum*, which causes the Far Eastern form of human schistosomiasis, is not peculiar to man but attacks domestic animals—cattle, horse, goat, dog, cat—as well. The six remaining species occur as natural infections in various animals, and some of these schistosomes may on occasion attack man, a point to be considered when investigating the origin of

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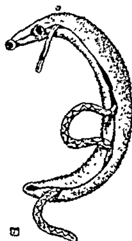
cercariæ are capable of causing a severe dermatitis without the development of visceral symptoms in those who bathe in infested waters. The habitat of these worms is the vascular system, and, in the adult form, *S. hæmatobium* is found in the portal vein and its branches and in the vesical, uterine, and hæmorrhoidal veins, while *S. mansoni* inhabits chiefly the

* *Schistosoma* Weinland 1858 = *Bilharzia* Cobbold, 1859.

longer and is more filiform (Fig 69). *S. mansoni*, though closely resembling *S. hæmatobium*, has certain structural differences. *S. hæmatobium* produces terminally-spined eggs, which are found usually in the urine, but sometimes in the fæces (Fig 71) The lateral-spined ova of *S. mansoni* are found usually in the fæces only, though rarely they may [illegible]

[illegible] cause of the symptoms. Work by Leiper and his colleagues has demonstrated the full life-history of the parasites and pointed the way towards prevention of the disease.

Fig 69.



Schistosoma mansoni, male and female within gynæcophoric canal. (After Looss.)

Fig. 70.



Lateral-spined egg of *S mansoni*

The egg, whether from the urinary passage or the rectum, if it reaches water, hatches into a ciliated free-swimming larva or miracidium which, unless it finds a suitable host, perishes in about twenty-four hours (Plate 28) The intermediate host—which, if found, it enters—is some species of fresh-water snail. In Egypt the whelk-like snail,* *Bulinus truncatus* (Plate 29 B), or the very similar *B dybowski* and *B innesi*, harbours the miracidium of the urinary *Schistosoma*, while the ammonite-shaped *Planorbis boissyi* (Plate 29 A) affords shelter to that of the intestinal worm A species of *Planorbis* (*P. dufourii*) was shown to be an efficient intermediary for *S. hæmatobium* in Portugal.

* According to Annandale, these three *Bulinus* are specifically identical, and should all be included in the one species, *B truncatus* *Bulinus truncatus* (Audouin, 1809)=*B contortus* (Michaud, 1831).

In the snail the larva becomes a sporocyst which gives off many daughter sporocysts, and these, in their turn, produce vast numbers of bifid-tailed cercariæ (Fig. 72) which escape into the surrounding water. A single snail has been known to discharge 170,000 of these at the rate of over 2,500 a day. These tiny creatures can just be seen with the unaided human eye when in clear water in a test tube. A lens is required for their detection in natural water. To the naked eye they look something like a swarming mass of tiny white hairs. Their expectancy of life in the free-living state is about thirty-six to forty-eight hours, and if they fail to get access to a human host within this time, they perish. They can penetrate the unbroken skin, and also pass through the intact mucous membrane of the mouth when being swallowed in water. The blood stream carries the cercariæ to the lungs, when they may pass directly into the liver by way of the diaphragm, or they may pass through the lungs, return to the heart, and reach the liver by means of the blood stream.

Fig. 71.



Terminal spined egg of *Schistosoma hæmatobium*.
(After Looss)

In the liver they develop into adult male and female worms, the process taking about two months to accomplish. Thereafter the females start producing the spined eggs.

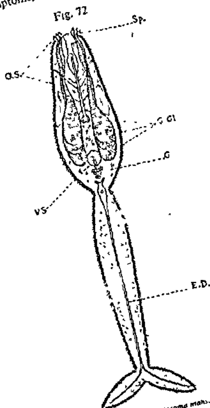
Symptoms.—These may be very slight or exceedingly severe. In primary

special kind. Work on an outbreak among Australian troops in Egypt (1914–18) showed that the incubation period of *S. mansoni* infection may vary from four weeks to three months. The most common period appears to be from four to eight weeks, a shorter time than in the vesical disease. *Some of the patients felt an itching of the skin on leaving the water where,* as events proved, they had been infected while bathing. The early toxic symptoms as a rule began gradually with loss of appetite, persistent headache, pains in the back and limbs, and dizziness. Cough was frequent and was sometimes the first symptom. Later, abdominal pain, enlarged

and tender liver and spleen, pyrexia associated with rigors and sweats, bronchitis, urticaria and diarrhœa were the chief features. The blood showed marked eosinophilia, but it should be noted that eosinophilia may be absent in schistosomiasis A distended abdomen with tenderness over the descending colon may be present.

Later the toxic symptoms, which are evidence of a heavy infection,

Fig. 72



Cercaria of *Schistosoma mansoni*

O S—oral sucker, V S—ventral sucker, Sp—Spines C Gl—Cephalic glands, G C—Germinal cells, E.D—excretory duct.

abate, and are usually followed by recurring attacks of diarrhœa and dysentery due to the ulcerative and polypoid lesions in the intestinal wall. The stools may be normal, and it may be very difficult to detect the ova. Remember that eggs may be easily found in scrapings made from lesions in the rectum when these are present. Cases have been known of prolonged schistosomal pyrexia in which the eggs were found *post mortem* only on scraping the bases of the intestinal ulcers (Fig. 73). In bad

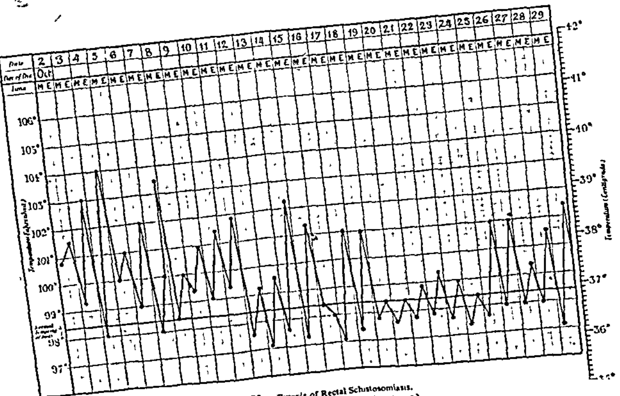


Fig. 73. Pyrexia of Rectal Schistosomiasis.
(4th Report, Wellcome Trop Res Laboratories.)

cases the lungs and liver suffer, the latter becoming cirrhotic, but as a rule there are no symptoms of such invasion. At the same time the urinary and intestinal trouble lead to invaliding from anæmia, marasmus, and the intercurrent diseases and sequelæ to which the victim of schistosomiasis is liable. In Africa *S. mansoni* is a common cause of splenomegaly and of a form of hepatic cirrhosis known as "pipe-stem" cirrhosis. Chronic schistosomiasis is also considered an important factor in the causation of Egyptian splenomegaly.

Diagnosis.—This depends on the microscopical examination of the urine or fæces and the finding of the characteristic eggs.

Sigmoidoscopy and cystoscopy, in their respective spheres, are often of great assistance in the diagnosis of schistosomiasis.

The complement fixation and dermal tests devised by Fairley may be helpful in establishing a diagnosis in doubtful cases.

Differential Diagnosis.—Care should be taken not to confound a chronic amœbic or bacillary dysentery with one due to schistosome infection. Rectal schistosomiasis had also to be distinguished from enteric infections, urticaria, pulmonary tuberculosis, and hepatic abscess. Appendicitis is another condition which it may resemble.

Treatment.—The specific treatment for schistosomiasis is the intravenous administration of sodium antimony tartrate, which in this disease is superior to the pentavalent compounds. It is usual to commence treatment of schistosomiasis with an initial dose of about ½ a grain of the salt. The injections are given every other day, with a maximum dose of 2 or 2½ grains. As the dose increases, some prefer to give the injections at two-day intervals. A course consists usually of about 20 to 30 grains in all, but, as in all other diseases which are cured by the injection of antimony, there is no universal curative dose, and each case must be judged on its own merits.

Emetine has definite curative properties in this disease, and is the treatment of choice for children where intravenous injections are difficult. For a child of nine years, Cawston recommends a total dosage of 9 grains, given intramuscularly, spread over twenty-four days, the maximum dose being ½ grain. Within the same period children of twelve years usually require 12 grains, and those of fifteen 15 grains to effect a permanent cure. Two-thirds of a grain, and 1 grain respectively, are the usual maximum doses. To counteract cardiac depression some such drug as sparteine (1/10 to 1/5 grain) may be injected along with the emetine.

As treatment takes effect, the ova passed out may be seen to be dark, shrivelled or distorted in appearance, and they do not hatch out when placed in water.

Anthiomaline, a lithium salt of antimony, is well reported on. Injection into the deltoid muscle of 4 c.cm. of anthiomaline on six days a week seems to have effected cure of *S. hæmatobium* infestation in two weeks among out-patients continuing their work, though reporting some generalized muscular pain. This would indicate that the eggs are disintegrated and the worms destroyed most readily by giving the drug sufficiently often to prevent their recovering from one dose before the next and before much of the drug already given has been eliminated.

With *S mansoni* infestations escape of the eggs is too uncertain to be much of a guide when treatment may safely be discontinued and 25–30 grains of tartar emetic is needed until such time as careful investigation has revealed the clinical equivalent of anthiomaline.

Stibophen (an antimonial preparation marketed by Bayer as *Fouadin*) is popular in Egypt. Its chief merits are that it is already made up and can be given by intramuscular injection. In Egypt, a 19-day course is used, in which the drug in 7 per cent. solution is given on alternate days; this course is said to cure over 97 per cent. of cases treated. The detailed procedure is 1·5 c.cm. (0 105 g.) on the first day, 3·5 c cm. (0 245 g.) on the second day, 5 0 c cm (0·35 g) on the third day, and again 5 0 c.cm. (0 35 g) on the 5th, 7th, 9th, 11th, 13th, 15th, 17th, and 19th days. Totals: injections=11, c.cm. of 7 per cent. solution=50, grammes of drug=3 5 If necessary four further injections may be given, each 5 0 c cm of 7 per cent. solution (0 35 g). Stibophen, 5 c.cm given i-m on five days a week for two weeks is also said to be effective.*

Prophylaxis.—This is most important and consists in the strict avoidance of any kind of personal contact with water which may by any possibility be infected The Nile and its canals, the lesser irrigation channels, the waters of swamps and marshes, and any permanent collections where the snail hosts may occur are to be viewed with suspicion.

Unfiltered water from such sources is dangerous unless it has been stored for at least forty-eight hours after being drawn.

Bathing, wading, washing and drinking in such waters must be forbidden

Clothes, unless waterproof, are no protection to the wader Gloves and more especially rubber gloves should be worn by those examining possibly polluted water for snail hosts or mosquito larvæ, while men such as engineers working in such water should be protected by rubber thigh boots and gloves

To ensure a safe water supply the following measures should be adopted —

(*a*) Weed on which the snails feed should be removed, and, if possible, infected water channels should be drained dry and sun-baked, the snails being killed by this means

(*b*) Chemicals, such as copper sulphate in amount equivalent to 1 lb. per 100,000 gallons (1 part per million), should be used for the destruction of snails.

(*c*) Snails may be eliminated from water supplies by means of a screen 16 meshes to the linear inch placed between the source and the intake

(*d*) Cercariæ, while not being eliminated by ordinary methods of filtration such as shallow sand filters, etc., may possibly be excluded by the Stellar and Meta filters, which are now fitted to army water trucks and trailers.

It should be noted that the apparent efficiency of filtration on a

* For full details of a two-day course with sodium antimony tartrate, particularly useful in mass treatment, *see* Alves and Blair, *Lancet*, 1946, Jan 5, p 8 *See* also pp 12 and 21 of the same issue

large scale, as for a town or city, is to be partly explained by the length of time intervening between the collection of the water and its consumption, which usually exceeds the minimum of forty-eight hours' storage required to ensure death of cercariæ It should be noted that sedimentation of water, with or without the use of chemicals, is not effective alone in dealing with cercariæ

(e) Certain chemical methods of destroying cercariæ are valuable. Superchlorination, as employed in the Army, kills the cercariæ in 30 minutes, chloramination in doses of 3 parts per million is effective in 60 minutes, while sodium bisulphate, 1 in 1,000, is immediately lethal

As regards the treatment of water not required for drinking purposes, cresol, 1 in 10,000, will render it safe immediately, if stored overnight 1 in 90,000 is sufficient

JAPANESE SCHISTOTOSOMIASIS
(Katayama disease, Oriental schistosomiasis)

Infestation with *S japonicum*, the cause of what the Japanese call katayama disease, is extremely prevalent in certain parts of the Far East, especially along the Yangste valley in north China It is also common in Formosa and Japan, on the borders of Burma, and in the Philippines and Celebes, it is also found in certain other parts

Individual infestations are apt to be very heavy The adult worm resembles *S hæmatobium* and *S mansoni* but the integument is non-tuberculated Seven testes can usually be distinguished in the male and the ovary in the female lies just posterior to the middle of the body. As many as 50 ova may be seen in the long straight uterus. The ova are oval and rather smaller (70 to 90 by 50 to 60 microns) than those of the other two schistosomes and have a small rudimentary spine or knob near one end which may be difficult to detect Species of the fresh-water snails, *Oncomelania*, *Katayama*, and *Schistosomophora* act as intermediate hosts

As in other schistosome infestations, man is infected by contact with water containing free-swimming cercariæ Three clinical stages may be recognized —

1 Incubation period and stage of larval invasion lasting about one month Skin irritation ("Kabure") and urticarial, pulmonary, and febrile manifestations are the usual features although they are inconstantly present

2 Stage of deposition and extrusion when the ova appear in the blood-stained stools Emaciation and dysenteric symptoms are marked The liver and spleen enlarge

3 This stage does not always follow, when it does it appears about three to five years after infection. It depends on heavy infestation and is marked by tissue destruction and reactionary proliferation of fibrous tissue Depending on the organs and tissues invaded, the features are . hepatic cirrhosis, usually with ascites and increasing splenomegaly, Jacksonian epileptiform attacks, amblyopia, severe dysenteric attacks, and so forth A chronic cachectic stage leading

With *S. mansoni* infestations escape of the eggs is too uncertain to be much of a guide when treatment may safely be discontinued and 25–30 grains of tartar emetic is needed until such time as careful investigation has revealed the clinical equivalent of anthiomaline.

Stibophen (an antimonial preparation marketed by Bayer as *Fouadin*) is popular in Egypt. Its chief merits are that it is already made up and can be given by intramuscular injection. In Egypt, a 19-day course is used, in which the drug in 7 per cent. solution is given on alternate days, this course is said to cure over 97 per cent. of cases treated. The detailed

Totals. injections=11, c.cm. of 7 per cent. solution=50, grammes of drug=3 5. If necessary four further injections may be given, each 5 0 c.cm of 7 per cent solution (0 35 g). Stibophen, 5 c cm given i-m. on five days a week for two weeks is also said to be effective.*

Prophylaxis —This is most important and consists in the strict avoidance of any kind of personal contact with water which may by any possibility be infected. The Nile and its canals, the lesser irrigation channels, the waters of swamps and marshes, and any permanent collections where the snail hosts may occur are to be viewed with suspicion

Unfiltered water from such sources is dangerous unless it has been stored for at least forty-eight hours after being drawn.

Bathing, wading, washing and drinking in such waters must be forbidden

Gloves

boots and gloves.

To ensure a safe water supply the following measures should be adopted —

(*a*) Weed on which the snails feed should be removed, and, if possible, infected water channels should be drained dry and sun-baked, the snails being killed by this means.

(*b*) Chemicals, such as copper sulphate in amount equivalent to 1 lb per 100,000 gallons (1 part per million), should be used for the destruction of snails.

(*c*) Snails may be eliminated from water supplies by means of a screen 16 meshes to the linear inch placed between the source and the intake

(*d*) Cercariæ, while not being eliminated by ordinary methods of ... be excluded ... water

It should be noted that the apparent efficiency of ... on a

* For full details of a two-day course with sodium antimony tartrate, particularly useful in mass treatment, *see* Alves and Blair, *Lancet*, 1946, Jan 5, p 8 *See* also pp 12 and 21 of the same issue.

large scale, as for a town or city, is to be partly explained by the length of time intervening between the collection of the water and its consumption, which usually exceeds the minimum of forty-eight hours' storage required to ensure death of cercariæ It should be noted that sedimentation of water, with or without the use of chemicals, is not effective alone in dealing with cercariæ.

(e) Certain chemical methods of destroying cercariæ are valuable Superchlorination, as employed in the Army, kills the cercariæ in 30 minutes, chloramination in doses of 3 parts per million is effective in 60 minutes, while sodium bisulphate, 1 in 1,000, is immediately lethal

As regards the treatment of water not required for drinking purposes, cresol, 1 in 10,000, will render it safe immediately, if stored overnight 1 in 90,000 is sufficient

JAPANESE SCHISTOTOSOMIASIS
(Katayama disease, Oriental schistosomiasis)

Infestation with *S japonicum*, the cause of what the Japanese call katayama disease is extremely prevalent in certain parts of the Far East, especially along the Yangste valley in north China It is also common in Formosa and Japan, on the borders of Burma, and in the Philippines and Celebes, it is also found in certain other parts

Individual infestations are apt to be very heavy The adult worm resembles *S hæmatobium* and *S. mansoni* but the integument is non-tuberculated Seven testes can usually be distinguished in the male and the ovary in the female lies just posterior to the middle of the body. As many as 50 ova may be seen in the long straight uterus The ova are oval and rather smaller (70 to 90 by 50 to 60 microns) than those of the other two schistosomes and have a small rudimentary spine or knob near one end which may be difficult to detect Species of the fresh-water snails, *Oncomelania*, *Katayama*, and *Schistosomophora* act as intermediate hosts

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to death in the usual termination. This third stage is specially characteristic of *japonicum* infestations.

Leucocytosis with eosinophilia (30–60 per cent.) is common during the invasion stage; this gives place to leucopenia with a normal or diminished number of eosinophils in the later stages.

Treatment with tartar emetic is usually effective in the early stages but is often ineffective in the later degenerative and proliferative stages and may even be dangerous when the liver is involved. Emetine, given by intravenous injection in daily doses of 1½ grains for 10 to 14 days, is said to be as effective as tartar emetic and less dangerous in the later stages.

SICKLE-CELLED ANÆMIA

Sicklæmia consists in a tendency, inherited as a Mendelian dominant,

also be seen.

Sickling is a reversible phenomenon directly related to oxygen concentration. The red cells are sickled when the hæmoglobin is in the reduced form, and they return to their normal discoid shape when it is combined as oxyhæmoglobin

The condition is seen three times more often in men than in women.

ulceration of the legs.

Pathology.—When the red cells assume bizarre forms the blood begins to stagnate in the vessels, causing anoxæmia and thus increased sickling. Thrombosis is found in end-arteries, and infarcts followed by necrosis appear in many organs. In children or adults dying after one or two hæmolytic crises the spleen is enlarged, showing areas of congestion and actual hæmorrhage round the central arterioles Later the hæmorrhagic areas are replaced by fibrosed nodules containing brown pigment, and after repeated attacks of acute anæmia the spleen becomes small and atrophied, sometimes weighing only 2–3 oz. The other organs are pale after death from acute hæmolysis, with small infarcts in the kidneys and lungs In the liver the intracellular canaliculi are distended with bile. The right side of the heart may be dilated. Osteoporosis of the long bones and thickening of the skull are not uncommon. The bone-marrow may also show hyperplasia, associated with the presence of fat emboli in various organs.

Symptoms.—During the acute hæmolytic crisis there is increasing pallor, [illegible]

marked and reticulocytes may form 25 per cent of the circulating reds. Phagocytosis of the red cells by circulating monocytes may be seen and a neutrophil polymorphonuclear leucocytosis of from 10,000 to 30,000 per c mm is usual Coagulation time and platelet count are normal A positive indirect van den Bergh reaction is obtained, with a raised icteric index

Anæmia, however, may not be the primary symptom There may, for instance, be severe abdominal pain which may simulate the gastric crisis of tabes, while patients suffering from sicklæmia have been mistakenly operated on for appendicitis, cholecystitis, and even perforated gastric or duodenal ulcer In other cases the heart sounds and cardiac enlargement may suggest mitral stenosis or other valvular lesions. Severe pain may *be felt in the muscles, long bones, and joints, mimicking acute rheumatism* except that the pain is not relieved by salicylates In some instances a single joint may become swollen and tender, with effusion into the cavity, and gonococcal infection may be wrongly diagnosed

Sicklæmia may also cause nervous symptoms, drowsiness or coma, hemiplegia, aphasia, headache, convulsions, stiffness or pain in the back and neck, irritability, weakness of the facial muscles, ocular disturbances, and cerebral vomiting Because the lesions are usually intracranial, and hæmorrhage is very rare, examination of the cerebrospinal fluid gives no reliable information though the fluid may be under increased pressure The relationship between sicklæmia and ulceration requires further study, as does the possible connection between sicklæmia and the not infrequent occurrence of jaundice in Africans suffering from lobar pneumonia

Diagnosis.—A drop of blood from the finger is placed on a clean slide and covered with a cover-slip The slip is immediately ringed round with vaseline or Canada balsam to exclude air. The sealed preparation is then kept either at room- or preferably at body-temperature and is examined microscopically at intervals up to 24 hours The rapidity with which sickling develops, and the percentage of red cells sickled in a given time, provides an indication of the severity of the condition. Normal blood will not sickle The test can also be carried out with oxalated blood.

Sickling in the blood-stream can be detected as follows 0 25 c cm of liquid paraffin is taken into a 2 c cm. sterile syringe, all air is expelled, 0 25 c cm of blood is then removed from a vein and immediately expelled into a test-tube containing 1 c cm of 10 per cent formalin in saline, *protected from the air by a layer of liquid paraffin.* The needle of the syringe is passed through the liquid paraffin into the formalin and the blood expelled. After allowing fifteen minutes for the red cells to be fixed they can be removed and examined microscopically. Sickling *in vivo* is usually associated with a hæmolytic crisis

Tissues removed *post mortem,* fixed *in formol and sectioned will show* sickle cells within the blood-vessels.

Treatment is purely symptomatic. With an acute hæmolytic crisis and a rapid fall in hæmoglobin repeated blood transfusion may be necessary. Where there is sickling but not anæmia administration of liver extract or yeast extract may decrease the chances of an acute hæmolytic crisis by rendering the bone-marrow less hyperplastic.

SKIN DISEASES

All manner of skin complaints occur in the sub-tropical and tropical areas. Even when trivial they are apt to be disabling Some, such as

the destructive *Ulcus tropicum*, a very serious complaint. Skin diseases are commonest and worst in damp and humid localities, but drier regions have their own special infections.

FURUNCULOSIS

Boils are troublesome in many tropical areas. Men are apt to suffer from them when they
hot climates tend to pr
have been very comm
Assam, and Burma.

Etiology.—The bacteriology of tropical boils has been the subject of a good deal of research. The most common organism associated with them is *Staphylococcus (pyogenes) aureus*—coagulase-positive.

Symptoms.—These do not require a lengthy description as everyone is familiar with the appearance of a boil. In the tropics they are often
Any part, however, which
on the face may
r blood-sucking
ir follicle.
ged course, continuing to discharge and refusing to heal As they are usually multiple, the unfortunate patient may be incapacitated for work.

Complications.—Lymphangitis and lymphadenitis may be mentioned.

Differential Diagnosis.—The occurrence of anthrax pustules following the use of infected shaving brushes must be kept in mind when a boil appears on the face, but the developed anthrax pustule is not like a typical boil and a bacteriological examination reveals the bacillus. When boils
examine the urine to exclude diabetes In
small boils may be caused
(Cordylobia anthropophaga)—see

Prophylaxis.—Protection from insect bites of all kinds should be ensured as far as practicable. First-aid treatment should be made

easily available for abrasions and other minor injuries sustained at games and other forms of recreation.

The provision and the enforcement of the use of adequate ablution facilities are important, while cleanliness of underclothing should receive constant attention with satisfactory laundering arrangements

It must be remembered that dietetic defects are often a factor in the causation of furunculosis and a sufficiency of vitamins in the diet must be ensured. Excessive consumption of carbohydrates, especially in warm climates, should be discouraged.

If a boil develops it should be covered with a small dressing to prevent spread to other parts.

Often the only effective preventive or therapeutic measure is a change of climate

Treatment.—When a boil is very small it may be aborted by injecting into its centre one drop of pure carbolic acid, or by dipping a sharpened wooden match or a toothpick into the carbolic and thrusting it repeatedly into the heart of the furuncle This method is painful but usually effective. If it is decided not to attempt to abort the boil it should be treated by heat, preferably by kaolin poultices. When suppuration occurs the boil may be opened by a small incision; and when the boil has been incised, 10–12 per cent sodium sulphate lotion may be used in order to promote drainage

Prompt application of penicillin cream (500–1,000 Oxford units per gramme) repeated 2- to 3-hourly will cause many boils to disappear This cream is also useful after incision if this has become necessary.

Vaccine therapy is of value in some cases of chronic furunculosis. Autogenous vaccines are preferable to stock preparations Fifty million organisms is a usual initial injection. Of the sulphonamide drugs, sulphathiazole or sulphadiazine in moderate dosage give the best results. A course of injections of penicillin is valuable.

It is important to raise the patient's resistance by giving him a carefully selected and well-balanced diet.

DESERT SORE

(VELDT SORE OR BARCOO ROT)

This is a chronic, septic, ulcerated sore occurring in hot, dry, sandy or desert parts of the tropics and sub-tropics. It occurs in the Middle East, South Africa, Iraq, the dry hot areas of India, and Northern Australia

Etiology.—The lesion usually forms on exposed skin, often at the site of an abrasion or insect bite It may be presumed that the affected skin has been devitalized by a combination of factors exposure to the sun, dust, and excessive sweating. Vitamin deficiency is often blamed but is probably not responsible A great variety of organisms have been isolated, including streptococci, diphtheroids, and staphylococci. A true diphtheria skin infection may occur in these sores.

Symptoms.—The lesion is usually found on the exposed parts of the body, especially the dorsal parts of the hands, forearm, elbows, knees

and occasionally on the face. It may begin as an *ordinary neglected* traumatic abrasion or as a painful vesicle which breaks down. The sore in the chronic stage is usually seen as a depressed circular or oval indurated ulcer with a sloughing base often filled with crusts of greenish pus and surrounded by a hard bluish or inflamed edge. There is usually little complaint of pain. These sores may persist for months if not properly treated.

Differential Diagnosis.—Oriental sore is distinguished by the presence of *Leishmania tropica*. A careful bacteriological examination should always be made to exclude any specific pathogenic organism.

Treatment.—*Prophylactic*—adequate washing and bathing facilities should be available for all ranks, special facilities being provided for mechanics, fitters, and others similarly employed. This may often be difficult to accomplish under field conditions but the highest attainable level of personal cleanliness must be aimed at even in the desert, where difficulties are very great. Daily application of a simple emollient cream may be useful in hot dry climates. Long slacks and shirts with full-length sleeves should be worn to protect the skin of the legs and arms against minor injuries of all kinds; special attention should be paid to measures of personal protection against insect bites (*see* Arthropod Pests and Appendix I).

Cuts and abrasions should receive immediate attention and should be kept covered by antiseptic dressings.

Curative—rest of the affected part, specific treatment of any pathogenic infection, otherwise treatment on ordinary surgical lines. Penicillin may be valuable.

ULCUS TROPICUM

This form of phagedænic ulcer in contradistinction to desert sore is met with in damp, steamy, tropical climates. The lower limbs are generally affected and a history of preceding trauma is common.

Etiology.—This is obscure. Some regard it as due to a dietetic defici-

Symptoms.—The seats of election for tropical ulcer are *the lower third* of the leg, the ankle, and the dorsum of the foot, *i.e.* parts liable to trauma. It may occur elsewhere and is known to produce *a form of ulcerative onychia.*

There is usually only a single ulcer, but two or more may occur.

The lesion begins as a small, tender, and often itchy papule or bleb with a dense inflammatory areola. An ulcer soon forms which is more or less painless and the edges of which tend to shelve and are not raised

funnel-shaped, the destruction being confined to the superficial parts. In certain cases after ten days or so the slough is thrown off and slow healing begins. Often, however, the disease attacks the deeper tissues and [illegible] fascia, tendons

Diagnosis.—In humid tropical climates a diagnosis is generally easy, though varicose ulcers, yaws, syphilitic, and blastomycotic ulcers may need differentiation.

Treatment.—On the assumption that there is a deficiency factor, a [illegible] should be given. Rest [illegible]

TINEA CRURIS

Tinea cruris (dhobie itch) is one of the commonest skin complaints of the tropics and was very prevalent in many war areas. It is worst during hot, damp weather, and may cause considerable suffering.

Etiology.—The eruption is usually caused by the fungus *Epidermophyton inguinale*, but occasionally other ringworm fungi may be isolated from the lesions.

Symptoms.—The crutch and the axillæ are the regions attacked. Intensely itchy, red, spreading patches develop which have characteristic raised well-defined margins, hence the old term "eczema marginatum" (Plate 32)

The irritation is worse at night, and often subsides during the cold weather, the areas affected becoming dry, scurfy and pigmented. The fungus is still present, though quiescent, and becomes active again under warm conditions.

Prophylaxis.—Wear clean cotton drawers, bathe frequently and use a dusting powder.

[illegible] to an ointment containing resorcin

powder. When the irritation is allayed, the painting may be recommenced if necessary. Reinfection must be prevented by wearing cotton drawers disinfected daily by boiling or by careful ironing.

Deck's ointment often proves efficacious :—

Ac. salicyl.	4	per cent.
Bism. subnit.	10	"
Hydrarg. salicyl.	4	"
Ol. eucalypt.	10	"
Lanoline and Vaseline to make up	100	"

(This ointment is very useful in some cases of *pruritus ani* and *vulvæ*, presumably of a parasitic nature. For this purpose dilute the ointment to half its strength to begin with.)

Bad cases require a 2 to 5 per cent. chrysarobin ointment employed with due warnings and precautions, and never prescribed when there is any renal infection. Dithranol, a substitute for chrysarobin, may be used as an ointment of 0 25 to 3 per cent. strength.

Interdigital Ringworm.—Epidermophyton not infrequently attacks the skin of the feet, particularly between the fourth and fifth toes. The disease may be spread through contamination of duck boards and of the floor or coconut mats around baths of all kinds. Football boots for common use and boots sent for repair and re-issued to other men may also spread the disease, occasionally, the re-issue of used blankets and socks is responsible.

[illegible]

football boats should be stored in an airtight box with a formalin-sprayed blanket at the bottom. Boots sent to workshops for repair should first be disinfected by exposure to formalin vapour in a special chamber.

TRICHOMYCOSIS CAPILLITI

[illegible] fungoid disease of [illegible] soldiers in the [illegible] ected, but, unless [illegible] unnoticed, and [illegible] es inflamed, the [illegible]

Etiology.—The disease is usually caused by *Actinomyces tenuis* (Castellani, 1912), which is a fungus having the ability to form a resistant, horn-like glue. On examining an infected hair microscopically under the low power, irregular rounded formations of a yellowish colour are seen; these

partially or totally encircle the shaft. Under the high power these for-

Actinomyces sendaiensis (Ping Ting Huang, 1933), which, in pure culture, is black in colour, has been isolated from twenty-five cases of trichomycosis.

Symptoms.—The incubation period is from two weeks upwards. Both axillary and pubic hairs may be affected, or either separately. Clinically, as indicated by the etiology, there are three types, Trichomycosis flava, T. nigra and T. rubra The hairs are seen to have a coated, beaded or nodular appearance, and the deposit on them is either black, yellow or red (Plate 34) The affected hairs break easily The adjacent skin may be affected and may be reddened or show a yellow discoloration.

Prophylaxis —Keep the axillæ shaved. As is well known, nearly all the natives of tropical countries shave the axillæ, and it would be a good thing if Europeans did likewise. Failing this, dusting with a mixture of powdered sulphur and fuller's earth is useful. Frequent changes of underclothing and bathing the parts liable to infection are helpful measures.

Treatment.—Shave the affected areas and apply either ung. hyd ammon. dil or sulphur ointment. Frequent applications of 1/1000 lot hyd. perchlor. or 1/3000 formalin solution are alternative measures. If the skin is inflamed use calamine lotion for a few days before employing stronger remedies.

In resistant cases, bathe the parts twice daily with a lotion containing 1 drachm of formalin in 6 ounces of rectified spirit, and apply 2 per cent. sulphur ointment at night.

The affected areas should be kept shaved for a period of four to eight weeks.

TUNGIASIS

The sand-flea, *Tunga** *penetrans*, the chigger, jigger, or chigoe was a veritable pest in the East African campaigns of the wars 1914–18 and 1939–45. Native troops and carriers, being well acquainted with it, usually deal promptly with it, but to many of the Indian troops it came as a new experience, and now and again neglected cases of chigger infection occurred. It was certainly a cause of inefficiency.

Etiology.—The insect (Fig. 74 and Plate 35, A) is rather like the common flea but smaller. It is red or reddish-brown in colour, and very active.

* *Tunga* Jaroki, 1838 = *Dermatophilus* Lucas, 1839.

full of ripe eggs, it is as big as a small pea (Plate 35, B and C). The eggs escape through the skin opening, hatch into larvæ, which spin cocoons from which in eight or ten days the fleas emerge.

Symptoms.—The feet are the parts most commonly infested, and chiggers are common between the toes and under the toe-nails. As troops

Fig. 74 —The Chigger Flea, *Tunga penetrans*


Male


Unmated female.


Pregnant female

often sleep on the ground, other regions are often affected. As a rule, [illegible]

in her burrow. Unless she is removed pus forms round the distended abdomen and the skin becomes inflamed, raised and swollen. In the middle of the little tumour so formed is a depression with the black dot (end of abdomen) at its centre. Once the eggs are discharged the skin ulcerates and the chigger is expelled. A small sore is left, which is very liable to infection with septic organisms and even with tetanus. Neglected sores accordingly go from bad to worse, and the ravages of chiggers in cases of multiple infection may be very severe and lead to death from secondary causes.

Prophylaxis.—Wherever possible, camps should not be formed in [illegible]

naphthalene is good, or a strong infusion of native tobacco. The latter may be used inside boots and shoes. Walking barefoot, and sleeping unprotected on the ground, should be avoided. A daily foot parade *should be instituted and strict attention paid to the cleanliness of the* feet. The following method of preventing the chigger gaining entrance to the skin is recommended as one which merits a good trial:—

Wash the feet thoroughly and then rub in a mixture consisting of 5 drops of liquor cresoli saponatus in 1 ounce of vaseline. Special care should be taken to treat in this way the spaces between the toes and the *under-surface of the toes. It is said that this method will afford protection* for three days. It has also the advantage that any chiggers which have penetrated the skin before its application are killed and can be more easily *and painlessly extracted than when alive.*

Treatment.—Chiggers are best removed under aseptic or antiseptic precautions with a needle or eye-spud. Long practice ensures the best results. The infected part is bathed with an *antiseptic lotion, and the*

little operation consists in widening the skin orifice with a sharp, clean needle, and freeing the chigger from the surrounding tissues in order to enucleate it whole. Then clean and dress the resulting lesion. If the chigger is ruptured it has to be removed by the aid of forceps, and this complicates matters and is a more painful procedure.

SLEEPING SICKNESS

(Trypanosomiasis)

Trypanosomiasis is endemic over about a quarter of the African continent, and in epidemic form has sometimes depopulated large areas. Before the present war about a million natives were treated for it every year. In West Africa, where it ranges from Senegal in the north to

A form of sleeping sickness known as Chagas' Disease is prevalent among infants and young children in South America. The causal organism is a trypanosome, *Trypanosoma cruzi*, and is transmitted by species of reduviid bugs of the genus, *Triatoma* (*See* Arthropod Pests.)

Etiology.—Sleeping sickness is the terminal stage of human trypanosomiasis, and there are in Africa two distinct clinical forms of the latter. The trypanosomiasis of the Belgian Congo, Uganda and Tanganyika Territory often runs a relatively benign course with little to indicate its presence beyond the palpable glands. This variety due to *Trypanosoma gambiense* (Plate 13) is carried mainly by two species of tsetse fly, *Glossina palpalis* (Plate 4) and *G. tachinoides*. Trypanosomiasis as found in Nyasaland and Rhodesia, due to *T. rhodesiense* (Plate 14), is a much more serious problem and a high proportion of those attacked develop the classical mental and neurological symptoms characteristic of the disease, from which they usually die, often within a relatively short time, unless diagnosed and treated energetically early in the course of the disease. The vectors of this variety are *G. morsitans* (Plate 3), and *G. swynnertoni*.

Many authorities, Kleine among them, consider *T. rhodesiense* and *T. gambiense* to be the same species with different degrees of virulence, while many also consider that *T. rhodesiense* and *T. brucei*, which causes "nagana" in animals, are identical.

The tsetse fly acts as a true intermediate host of the trypanosome it transmits. It is not merely a mechanical vector. In all probability the lymphatic system is quite as important a habitat of the trypanosomes as the blood. The parasites produce a toxin to which in part the symptoms are due. The incubation period in man is not definitely known. It is probably about three weeks.

Symptoms.—The fly bite causes a slight local irritation which soon subsides, and a little later the disease begins insidiously with an irregular, intermittent fever which may be accompanied by a curious, patchy erythema, best seen on white skins. It is sometimes annular and is of a

fleeting nature. Localized œdema may appear and hyperæsthesia present. Cardiac excitability may be noticed and slight splenic enlar ment. The fever subsides only to recur, perhaps after a long interv Gradually the patient grows weaker, he suffers from headache, his cervic glands and other lymphatic glands begin to enlarge and may be tende At first soft, they become indurated later. The blood shows sligh anæmia. In some cases the spleen becomes very large and the liver ma increase in size. This is the first stage, that of trypanosome fever, and i may end in recovery. More commonly the cerebral stage, that of sleeping sickness, develops, but it may not make its appearance for years. Usually it occurs in from four to eight months. It may commence with acute, even maniacal symptoms, but as a rule there is merely an increase of the weakness and languor. The patient becomes dull and disinclined for exertion, he walks slowly and has a shuffling gait. His face grows puffy and wears a sulky or vacant expression. He becomes drowsy, exhibits tremors of various kinds and suffers from a dull headache, which at times, however, is very severe. Marked nocturnal insomnia is often a feature at this stage. He still has fever, the temperature running up at nights, and ere long he becomes a hopeless invalid, lying helpless and indifferent to his surroundings though still capable of being roused and of speaking and swallowing. Still later he will fall asleep with half-masticated food in his mouth, and as time goes on he loses flesh, the tremors increase, he is seized with convulsions, his neck muscles may become rigid and his head retracted, so much so that, at this stage, the condition may be mistaken for cerebro-spinal fever. Trophic changes set in, there may b paralysis, the lips become swollen and saliva dribbles from the mout Incontinence of urine and fæces sets in, and if an intercurrent infectic such as pneumonia or dysentery does not terminate the scene, the patier becomes comatose before the end or dies of exhaustion.

The severe nervous symptoms coincide with the entry of the trypanosomes into the cerebro-spinal system.

The form due to *T. rhodesiense* runs a more rapid course than Uganda sleeping sickness and appears to be almost invariably fatal unless treated energetically in the early stage. Very often there is no enlargement of cervical glands.

Diagnosis.—During the first . . .
of the causative parasit . . .
juice. They are not, as . . .
the trypanosomes can still be found . . . either. In the cerebral stage . . . gland
at the pre-agonal period, and they are also present in the cerebral stage
fluid and can usually be found in the blood, often in large numbers
some has also been f . . . after centrif . . . present in the cerebro . . . spinal
Inoculation . . . pano-
dog, or guinea- . . . (*Cercopithecus*),
also be used to test the efficacy . . . aid in diagnosis, and this method may
of treatment.

It must be understood that large numbers of trypanosomes may be present in the brain and yet absent from the blood and cerebro-spinal fluid when examined microscopically or tested by animal inoculation. Therefore such negative findings cannot be taken as absolute proof of

freedom from trypanosomiasis, whether the tests are employed as a diagnostic measure, or as a control in treatment.

Differential Diagnosis.—Malaria, kala-azar, some forms of cerebral syphilis, especially general paralysis, and pellagra may be mentioned as diseases from which trypanosome fever and sleeping sickness must be distinguished.

Glandular enlargements, especially of the posterior cervical region, in persons who have lived in or visited a trypanosomiasis endemic area must always be looked on with suspicion and gland puncture should always be carried out if necessary. The method of obtaining the specimen is simple, a gland is fixed with one hand and a perfectly dry, medium-bore needle is pushed into it with the other, twisting the needle will break down a little tissue, and gentle pressure on the gland will force the cellular debris up the lumen while the needle is slowly withdrawn The specimen is examined unstained and the trypanosomes are seen in motion, for the experienced observer the diagnosis is then relatively easy but if the specimen is blood-stained the movements of microfilariæ may mislead the unwary. Staining by Leishman or Giemsa will clear up any doubt.

The serum-aldehyde test introduced by Napier for the diagnosis of kala-azar has given positive results in a high proportion of individuals suffering from trypanosomiasis, likewise, the sera of trypanosomiasis patients are often found to contain a significant titre of "cold agglutinins" —antibodies that may be found in low titre in normal sera and in high titre in primary atypical pneumonia. Heterophile antibody (Paul Bunnel reaction) may also be increased beyond the usual limit for normal human serum

Prophylaxis.—General prohpylaxis is too large a subject for consideration here. It involves amongst other matters the question of the rôle of big game as reservoirs of infection. Personal prophylaxis consists in protecting against the bites of tsetse flies (*see* Arthropod Pests) A single dose of a curative drug such as Antrypol may give a few months' protection

Treatment.—The most effective drugs in the early stages are certain complex urea preparations, of which the best known are Bayer 205 (Germanin*), the French drug 309 (Moranyl), first synthesized by Fourneau, and the British Antrypol (B D H). These may be administered intravenously in 1 gramme doses dissolved in 10 c cm. of distilled water, the injections being given once a week. A total of 10 g. may effect a cure.

Experience shows that better results may be obtained by giving the first three doses more closely spaced, say on the 1st, 3rd, and 5th days, the subsequent doses being given weekly. There is some doubt whether

* British equivalent—Suramin.

As this preparation may give rise to albuminuria, the urine must be watched carefully during treatment. If this complication should unfortunately occur, it does not necessarily contra-indicate further treatment.

Where there is evidence of involvement of the central nervous system,

hich is administered intra-

nefit. Commence with 1 g.

with a dose of 2 g. once a

week until twelve doses have been given. In a patient who has already been treated vigorously with arsenic, it is better to employ Bayer 205 instead of tryparsamide, for the parasites may have become arsenic-fast, and, moreover, there is a danger that the further administration of an *arsenical preparation may give rise to ocular changes.*

McQueen has used a combined course of antrypol (Bayer 205) and tryparsamide in the treatment of Nigerian natives infected with *T. gambiense*. After a test dose of 0·2 g. of antrypol he gives three injections each of 1·0 g. of antrypol followed by five injections of tryparsamide, each of 2·0 g. every *fifth day in distilled water. In advanced cases, ten such* injections of tryparsamide are given.

SMALLPOX

(Variola)

It is not intended to deal with smallpox in quite the same manner as other diseases are treated in these Memoranda. Aberrant forms of smallpox occur in the tropics, such as the so-called Amaas or Kaffir

This is very like mild smallpox,

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Diagnosis.—The medical officer should always bear in mind the possibility of smallpox, and be suspicious of a disease commencing with a *chill* and continuing with high fever, severe headache, severe pains in the back and vomiting. He should remember that the broad features of the *smallpox rash* are that "it prefers the upper half of the body to the lower, that it is a rash of the face and arms rather than of the trunk and

Prodromal rashes, although uncommon, are of great value in early diagnosis if their significance is appreciated because they precede the

smallpox eruption by several days. They are most often to

One of the chief difficulties is to decide whether a case is smallpox or chickenpox, and the difficulty is apt to be greater when dealing with a dark skin There is no single characteristic sign on which absolute reliance can be placed, and it is often extremely difficult to distinguish moderately severe chickenpox from mild smallpox. Under war conditions it is well invariably to vaccinate and regard the condition as smallpox

It is always helpful to mark out an area, the so-called skin window, and observe the character of the rash within it, whether the eruption is all more or less at one stage as in smallpox or there is evidence of successive crops as in chickenpox

The following remarks by Thomas are likely to prove helpful. He says that "the greater depth of the initial skin lesion in smallpox explains —

(1) The shotty character of the rash, (2) the pearly-yellow contents of the vesicle, the colour being due to the thicker epithelial covering, (3) the hardness and hemispherical surface of the vesicle, (4) the absence of the crenated edge in the vesicle. This is possibly damped out by the thicker layer of epithelium, just as the several layers of an onion hide the irregularities at the core, (5) the absence of early cupped scabs owing to the difficulty of rupture, (6) the pitting, (7) the thickness of the crusts, (8) the presence of 'seeds' in the palms and soles, (9) possibly the umbilication and the formation of septa "

"The superficial position of the lesion in chicken-pox explains —

(1) The moderately soft character of the rash, (2) the clear transparent, almost colourless contents of the vesicle, due to the very thin epithelial covering, (3) the soft and sometimes spherical or ellipsoidal surface of the vesicle, (4) presence of crenation or puckering in the vesicle; (5) early cupped scabs, (6) the absence of pitting, save in severe cases, (7) the thinness of the crusts, (8) the absence of 'seeds' in palms and soles "

In the tropics, chickenpox is often relatively severe and the lesions may be profuse with considerable spread to the face Infrequently, the lesions of chickenpox may be found on the soles and palms but even in these situations they tend to lie *on* rather than *in* the skin and never have the hard shotty feel of the corresponding smallpox "seeds". Severe cases of this type often give rise to difficulties in differential diagnosis, especially if there is much constitutional disturbance– as there may well be with chickenpox in a non-immune community

Distribution of rash —In such difficult cases, special attention should be paid to the general distribution of the rash, which must be viewed with the patient stripped and in a good light. If the body is viewed as a whole it will very rarely be found that the rash of chickenpox is other than centripetal, or the rash of smallpox other than centrifugal Too much reliance must not be placed on the time interval between the onset of fever and appearance of the rash or on whether the rash appears, more or less, all at the same time or in successive crops. Ricketts has said "In broad terms the rash begins at the top and travels downwards. In the mildest sorts of cases the whole rash may be out within 24 hours . . on the other hand in severe cases the lapse of 48 hours may hardly see the

last arrivals . . . the outcrop is a gradual process not only over the whole body but also in any one particular part. In such circumstances the patient may exhibit on the first day of efflorescence a scanty rash on the face and upper part of the body only . . . In every epidemic cases will arise at intervals in which the eruption is so highly modified and the character of the lesion is no anomalous that there is an inadequate basis for diagnosis . . . yet it must not be forgotten that it is not possible for discordant distributions to *run in series also.*"

The chief difficulty arises when only a few scattered lesions are to be seen It must also be remembered that certain aspects of syphilis, especially in dark-skinned races, have to be distinguished from smallpox, *which at times they rather closely resemble. Careful inquiry and inspection* will usually clear up the diagnosis. Appropriate laboratory tests for

below).

Laboratory Diagnosis of Smallpox.—Early diagnosis of smallpox is often difficult on clinical grounds, and laboratory methods hitherto available have involved a good deal of delay, special skill, and difficult technique; now a much simpler method has been described in detail by van Rooyen. This involves microscopic demonstration of the characteristic masses of Paschen bodies in scrapings from the skin lesions of smallpox; a positive result may be obtained as early as the third day of illness when the rash appears.

guidance on interpretation and wording of reports. In the article referred

The first step is for clinicians and pathologists to try out the method together. The pathologist must learn, by studying typical cases of

both clinician and pathologist have gained confidence in their application

Skilfully used, this test should prove of great value especially in early and mild cases of smallpox since a firm laboratory diagnosis may be made

* *British Medical Journal*, 1944, Oct 21, 526.

before this would be possible on clinical grounds alone. After the skin lesions have progressed through the papular and vesicular stages and have become pustules, the Paschen bodies tend to disappear, but by this time the clinical picture should be sufficient for diagnosis.

It has not been thought advisable to describe the technical details, or the advice on interpretation and reporting of films, because, in this instance, brevity might open the door to misunderstanding. For these particulars, reference should be made to the original article, which is admirably explicit and wisely insistent on the need for practice before the method is adopted by any who have not already had experience of its use.

Prognosis.—Smallpox in the Far East and Middle East, and in the tropics generally, is apt to be a grave disease with a high mortality among those not adequately protected by *recent successful vaccination*—that is, vaccination with vesicle formation. *Hæmorrhagic* and *confluent* forms are responsible for the great majority of deaths due to smallpox. Confluent smallpox is usually diagnosable on sight (Plate 37), but hæmorrhagic forms may present great diagnostic difficulties if the possibility of smallpox is not kept constantly in mind. The hæmorrhagic tendency often develops early in the disease and the patient may die before the characteristic smallpox eruption has evolved or while it is still in the larval state. A bloated appearance of the face is a valuable sign in these early hæmorrhagic cases. The early papular lesions can be felt with the fingers before they become visible. Diagnosis such as acute lymphatic leukæmia, scarlet fever (on account of the early prodromal erythema), and hæmorrhagic measles have been first proposed for cases that later proved to be hæmorrhagic smallpox. A much-less-fatal, though still severe, form of hæmorrhagic smallpox may be seen in which some, or many, of the individual smallpox lesions develop a hæmorrhagic tendency after they have first appeared as normal lesions.

Treatment.—There is good evidence that a 5 per cent. solution of permanganate of potash painted on the skin of smallpox cases, or used as a bath, mitigates the severity of the disease, and also lessens the risk of infection.

An extensive trial with sulphonamides (chiefly sulphanilamide and sulphathiazole) has given conflicting, but on the whole disappointing results. It was hoped that sulphonamides would lessen the incidence and severity of secondary skin infections and consequently diminish the tendency to unsightly pocking and secondary toxæmia and fever. Early reports were optimistic, but later reports have failed to confirm our first hopes.

Penicillin, on the other hand, has apparently had greater success. Its use has appeared to save the lives of several gravely-ill, confluent cases of smallpox, but the numbers so treated are still too small for a dogmatic pronouncement of its value in this connection.

Vaccination.—The usual faults in technique are lack of cleanliness causing sepsis, the use of antiseptic for cleansing the skin (soap and water and a nail brush, followed by careful drying with a perfectly clean towel, sterile if possible, will meet the case), overheating of the lancet needle or scarifier when sterilizing it, drawing blood, exposure of the recently-

vaccinated area to the hot sun (a very important point in the tropics) or covering it with a dressing before the lymph has dried, charring of the lymph in the capillary tube when sealing [illegible]

[illegible] the Army is done with one [illegible]

or [illegible]

all [illegible]

th [illegible]

carried out at varying intervals between one and five years according to the estimate of local risks within the Command area. Three incisions, with 1 inch between each, are used in face of an epidemic, when all at risk are vaccinated unless done within the previous 14 days. In the event of failure at the first attempt with one incision, a further attempt is made after a week, using three incisions.

Three types of reaction are possible: immediate, accelerated, and primary (normal take).

Immediate.—A raised area of erythema appears round the insertion and reaches a maximum within 72 hours of vaccination; it disappears rapidly, without vesicle formation. This reaction is an indication of sensitization acquired from previous vaccinations; it is not to be regarded as a criterion of successful vaccination. It does not necessarily indicate immunity—though often given by immune subjects. By an unfortunate misnomer, the immediate reaction has often been referred to as the immune reaction—a term that, as Marsden emphasizes, has been the cause of serious misunderstanding and should be discouraged.

Accelerated.—Maximum intensity is reached within seven days of vaccination. It is usually pustular on the fourth to fifth days. This type of reaction is given by previously-vaccinated subjects.

Primary.—Maximum intensity is reached after the seventh day following vaccination. This type of reaction is that normally given by those vaccinated for the first time or those previously vaccinated whose immunity to vaccinia (not necessarily their immunity to variola) has fallen off completely or to a marked degree.

[illegible]

The papule is small, round, flat, bright red, [illegible] the fifth day the summit of the papule becomes vesicular. The vesicle is at first clear and pearl-like. Umbilication soon develops as the vesicle enlarges. A deep, red, and swollen areola surrounds the vesicle and grows wider as the lesion advances. This gives the picture of the 'pearl upon the rose leaf' which constitutes the true Jennerian vesicle. By the [illegible] umbilicated

feels hot, is painful, and the axillary glands become enlarged and tender. About the ninth day the areola begins to fade and the swelling subsides. By the eleventh or twelfth day the vesicle rapidly dries, leaving a brown, wrinkled scab, which finally drops off. It should never be removed, as it forms the best bandage.

"The scar is at first red, finally white, with the pits or foveations so characteristic of true cowpox."

A practical point of some importance is to see that the vaccinee does not deliberately remove the vaccine lymph after vaccination. A tragic case is on record in Egypt where a soldier did so, licking off the lymph with his tongue. Not long afterwards he developed a severe attack of smallpox and died of the disease.

It is of the greatest importance to observe scrupulously the instructions for the cool storage and early use of lymph. In ordinary circumstances lymph must be used within seven days of the "date of manufacture" stamped on the label, but if it can be stored in a reliable refrigerator this period may be extended to 14 days.

Intradermal methods of vaccination are in vogue in some countries but are not in favour in the British Army.

SPRUE

In the East sprue is common in South China, the East Indies, India and Ceylon, and in the West, the West Indies and the Southern United States For some reason so far unexplained, the disease is rare in Tropical Africa Although sprue had not previously been reported in Egypt, a few typical cases were seen there during the 1939–45 war. Most were among troops stationed in the Western Desert and living on a monotonous diet with little fresh food of any kind. A sprue-like syndrome was also noted as an occasional sequel of prolonged chronic dysentery, especially in recently-captured German prisoners of war, before capture many of these men had remained on duty in the front line for many weeks, either in the Western Desert or elsewhere, although they were suffering from chronic dysentery. Occasional cases have been seen in North Africa, Greece, and Italy. Usually it affects those who have been long resident in endemic centres, but long residence is not so important as had been supposed, some developed classical sprue after a few weeks in India

Etiology —The cause of sprue is unknown. Hamilton Fairley attributes the disease to a metabolic breakdown of the gastro-intestinal tract of unknown etiology and considers infection to be an unlikely cause The view that the responsible agent is a yeast has been generally abandoned, though it is possible that some part of the intestinal symptoms may be due to invading fungi, and it must be admitted that certain etiological factors connected with the disease fit in well with the theory of a chronic intestinal infection in some way connected with a warm humid climate.

H H Scott noted the incidence of tetany in many cases of sprue and advanced a theory of parathyroid deficiency with resulting hypocalcæmia. Consequently, he advised parathyroid tablets and calcium as part of the treatment. It is now realized that the hypocalcæmia with resulting

tetany is due to malabsorption of calcium and *not* to parathyroid dysfunction.

The combination of fatty acid with phosphoric acid is believed to be an essential step in the absorption and transport of fat, and Stannus has suggested that this phosphorylation of fatty acids fails in sprue, the failure being primarily due to lack of vitamins of the B group. The *dramatic action in cases of sprue of crude liver extract given parenterally* is explained by the fact that it contains the known and unknown constituents of the vitamin-B group which catalyse the process of phosphorylation. Folic acid may be important

Leishman has suggested that sprue may be the result of a disturbance of this equilibrium in the small intestine, due to a change in the proportion or type of flora or to a change in the intestinal media such as might follow unaccustomed diet or altered gastric acidity.

A disturbance in liver function appears to be responsible for the earlier symptoms, while the late starvation signs are accounted for, in some cases at least, by degenerative changes affecting the intestinal villi and glands. In other, apparently typical cases, no such degenerative lesions are found at autopsy and the cause of the wasting is obscure. Fat absorption is markedly diminished and some think there is an actual excretion of fat from the body. *The developed disease is a picture of multiple nutritional* deficiencies.

Symptoms and Morbid Anatomy

Symptoms at Onset.—In at least several of the endemic areas there is a form of diarrhœa common during the hot humid season, and seemingly quite distinct from mild dysentery. The diarrhœa is usually accompanied by some digestive disturbance and perhaps flatulence, and is characterized

months, or a short sea voyage may have the same effect. In the majority

when a sprue patient fixes the commencement of his symptoms at some definite time, a cross-examination will often bring out a history of *dyspepsia* and looseness of the bowels antedating the supposed onset by months or years.

In other instances sprue follows dysentery, either bacillary or amœbic, and if the latter, amœbæ may be found in the typical sprue stools The sequence of sprue on *hill diarrhœa is so frequent* as to suggest some etiological relationship between the two conditions. Again, the onset may be acute, and an attack of what seemed to be a simple diarrhœa quickly assumes the characteristic features of sprue. In yet other cases

emaciation without other complaint may be the presenting symptom. Soldiers may sometimes be picked out on a routine parade on account of their obvious emaciation, who stoutly deny that there is anything whatsoever wrong with their health, although they may have lost several stone in weight in as many weeks. Subsequent investigation of these individuals has, however, shown them to have been suffering from typical sprue, and one wonders how they could have carried on so long without complaint or apparent inconvenience. Emaciation without corresponding debility is characteristic of at least one type of sprue in its early stages. Cases of this type usually do well on a regulated simple sprue diet and may not even have to leave the endemic area

Symptoms of Established Disease.—These symptoms are best considered in groups

Stomach and Intestine —The patient complains of indigestion, and of flatulence, affecting both the stomach and intestine as evidenced by eructations, borborygmi, and distension. In advanced cases the feeling of abdominal tension may be so severe as to incapacitate the sufferer until the gas can be expelled. There is looseness of the bowels, usually not of a marked degree, two or three motions being passed during the morning, and perhaps no more for the rest of the day. The motions, especially the first in the day, are often passed with explosive violence, and the call to stool may be sudden and imperative. Occasionally diarrhœa is more marked, and pale, watery, bubbly stools are passed every couple of hours or so throughout the day. Any pre-existing anal trouble, such as hæmorrhoids or fissure, tends to become aggravated, and may constitute the patient's chief complaint Typically the stools are pultaceous, light coloured or white, foul-smelling, and blown out with gas Fermentation is so active that if a specimen is left in a corked tube, the cork may be found later blown out They are very bulky, so that the patient may wonder how with so small an intake he can pass so much The total fat in normal fæces is under 25 per cent of the dry weight, often much lower, but in sprue it is increased to 30, 50, 60 per cent. or more Typically the fatty acids are increased in proportion to the neutral fat, N F 1 F A 3 to 5 or occasionally 7, instead of the normal N F. 1 F A. 2 In pancreatic disease the ratio may be N F 15 F A 1, owing to defective fat-splitting (Thompson) The results of fat analysis, however, are subject to variation depending on the rate of passage of food through the intestinal canal, the time that elapses before the specimen is examined, and the effect of heat if the material is dried by this method so that otherwise typical cases of sprue, which react at once to treatment, may not show the fatty constituents present in the proportion stated

Mouth.—There is thinning of the mucous membrane of the mouth and tongue, with patches of congestion, vesicles, and small superficial ulcers. These are seen on the tip, edges, and under-surface of the tongue, inside the lips and cheeks, and sometimes on the palate and in the throat The lesions tend to appear in crops, and may render mastication an agony to the patient The accompanying irritation leads to increased salivation and sometimes actual dribbling There may be areas of superficial erosion, most easily seen if the tongue is protruded and allowed to dry,

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It has been shown that thiamin, riboflavin, nicotinic acid, and biotin

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SYMPTOMS AND MORBID ANATOMY

Symptoms at Onset.—In at least several of the endemic areas there is a

months, or a short sea voyage may have the same effect. In the majority of cases such a diarrhœa gradually passes off, or at least is tolerated, but in some small proportion the condition progresses, the symptoms becoming more sprue-like, until finally typical sprue supervenes. Even when a sprue patient fixes the commencement of his symptoms at some definite time, a cross-examination will often bring out a history of dyspepsia and looseness of the bowels antedating the supposed onset by months or years.

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when glistening patches not otherwise apparent are easily detected. The surface of the tongue may look red, raw and shiny, and resemble a raw beefsteak in appearance. It is smooth owing to atrophy of the filiform papillæ, while the fungiform *papillæ may stand out red and enlarged.* Especially in chronic cases the surface of the tongue may show the presence of fissures. In spite of the dyspepsia it remains clean.

When these changes are extensive the appearance of the tongue eventually conforms to one of two types: "the smooth magenta tongue" or "the scarlet raw-beef tongue". It is tempting to ascribe these lesions to deficiency of riboflavin or nocitinic acid, but as yet there is no real proof that this is correct.

Mouth symptoms may be a very early feature, and a patient who shows little else wrong may complain that certain pungent articles of diet "sting" his tongue. On the other hand, a sore mouth may suddenly develop after two or three years of otherwise typical sprue. And again, the disease may run its whole course without lesions in the mouth.

Blood.—Some degree of anæmia is present in established sprue, and a red cell count of 3½ million or 4 million per c mm. would be an average finding in a case of moderate severity. In severe cases the blood picture [illegible]

enough form, the bone marrow undergoes toxic degenerative changes, including even complete aplasia, with a resulting fatal aplastic anæmia, characterized by a falling red cell count, and no sign in the peripheral blood of attempted regeneration. It is always a grave sign if anæmia increases after the gastro-intestinal symptoms have definitely improved.

The white-cell count shows some reduction, but not an actual leucopenia unless the anæmia is very severe. There is a relative increase of lymphocytes at the expense of the polymorphonuclear cells.

Mental Changes.—In proportion to the severity and duration of the illness mental deterioration is present, often not obvious to the patients themselves, but noticed by their friends or fellow workers. Lack of concentration, infirmity of purpose, depression, irritability, and unreasonableness may be in evidence. They are slow in answering questions which require thought, *but once under way they may be tryingly garrulous.* They are introspective, and, if persons of intelligence, delight in analysing their symptoms, and may be full of knowledge, of a sort, regarding sprue.

General.—There is increasing loss of *weight, and in advanced cases the* sufferer may be reduced to the classical condition of a skeleton with a blown-out abdomen. The organs share in the general wasting, so that *the area of liver dullness is much* decreased. The temperature is subnormal and the patient *abnormally sensitive to cold, and in some cases* cramps and even tetany may occur. The skin is pigmented, especially that of the face and forehead. Generalised œdema may mask the loss of flesh.

In a proportion of patients with sprue, vitamin-deficiency changes are seen in the skin of the limbs, usually of the legs. These are: follicular hyperkeratosis from lack of vitamin A, which causes a "toadskin"

appearance, and parakeratosis from lack of vitamin B, which causes an appearance like "cracked parchment".

Peripheral neuritis with sensory changes is a not-uncommon complication of long-standing sprue, especially if accompanied by severe anæmia. In patients whose anæmia is macrocytic in type the differential diagnosis from subacute combined degeneration of the cord may present real difficulties.

If not checked by treatment the disease drags on its weary course, interrupted by temporary remissions which are followed by relapse, wasting and debility increase, and the patient dies of starvation, anæmia, or some intercurrent disease

Morbid Anatomy.—The most characteristic changes are found in the intestinal mucosa which shows areas of thinning, rarely accompanied by ulceration, this being part of the general wasting process and not a necessary part of the sprue syndrome The villi and glands are involved in the degenerative process, and the affected villi appear shrivelled, or may undergo complete atrophy and replacement by cicatricial tissue. The muscular coat is also atrophied The erosions of the mucous membrane may be present throughout the alimentary tract, more or less generally, or in patches, or restricted to some part In some apparently typical cases, however, no obvious intestinal changes are seen *post mortem*.

The bone marrow shows characteristic changes In many cases the interior of the long bones is filled with red marrow and there is a megaloblastic hyperplasia A peculiar gelatinous appearance of the yellow marrow, also seen in other intestinal diseases, is said to be characteristic The liver, spleen, and kidneys often give the Prussian blue reaction due to the deposition of hæmosiderin

Diagnosis and Prognosis

Diagnosis The combination of flatulent dyspepsia, pale frothy stools, sore mouth, and loss of weight, often extreme, presents an unmistakable picture, but this diagnostic tetrad may not be complete, and diagnosis and treatment should never be postponed because, for instance, mouth lesions are absent, or there has been no serious loss of weight Larval sprue is a common and widespread condition and often escapes detection. The subject may complain only of some dyspepsia and flatulence, and perhaps is found to pass one or two pultaceous stools daily If these show any loss of colour, or if the total fat is increased, the patient, however mild the symptoms, should be confined to bed, thoroughly investigated, and, if necessary, treated as a case of sprue A speedy response encourages persistence with the treatment Do not handicap him in his career by making an official diagnosis of sprue if this is reasonably in doubt, but never postpone or withhold treatment on this account Many persons suffering from classical sprue give a history of mild symptoms, like those mentioned, which persisted undiagnosed for months or years before progressing to the text-book picture

Differential Diagnosis. The result of chemical analysis of the fæces is usually helpful in distinguishing between chronic pancreatitis and sprue

In the former there is defective splitting of fats, while in sprue the process goes on actively, even to excess. Pancreatitis does not give rise to mouth symptoms, nor does the disease react to treatment in the striking manner common in sprue The intestinal symptoms of pellagra may resemble those of sprue, but the development of erythema of the face and hands will prevent confusion. The history of the case, the later development of severe anæmia, and the usual absence of megaloblasts will distinguish from pernicious anæmia. Hill diarrhœa that does not clear up should be regarded as sprue. A useful pointer to sprue is the different shape of the glucose-tolerance curve depending on whether the glucose is given by mouth or intravenously. Because of poor absorption the curve after oral glucose tends to be flat, whereas in the same patient after intravenous glucose it assumes a normal shape.

Radiological appearances.—A plain X-ray of the abdomen reveals abnormal quantities of gas in the small bowel and colon, and a large mass of fæces in the colon. The barium meal reveals changes of the mucosal pattern and in the muscle wall of the small intestine, these are most marked in the middle third

In the early stages the mucosal folds become coarser and less frequent in number. The fine feathery pattern of the small bowel is thus replaced by a course irregular pattern (Plate 12). In later stages, atrophy of the mucosal folds progresses to such a degree that the pattern completely disappears.

Changes in the muscle wall become apparent radiologically because of alterations in the tone of the small bowel Alternating areas of hyper- and hypo-tonicity interfere with the normal peristalsis of the small bowel and give rise to a curious segmented appearance which has been likened to a "string of sausages". The general result is a delay in passage of the meal through the stomach and small bowel. These changes constitute the "deficiency pattern". In themselves they are characteristic, but they must not be regarded as diagnostic of sprue.

Prognosis.—The age of the patient and the duration of the disease are important factors. Young adults as a rule respond more readily to treatment than persons past middle age. The earlier a patient comes under treatment the more hopeful is the prospect, for in cases of long standing the intestine may have suffered irreparable damage with destruction of villi and glands. Persisting anæmia of a severe grade is a grave complication, for it is evidence of hypoplasia of the bone marrow with the ever-present danger of the development of aplastic anæmia.

When treatment has effected a clinical cure, the ultimate prognosis is affected in a large degree by economic considerations. If circumstances permit of such persons remaining at home, the position is very hopeful On the other hand, if they must return to an endemic area, the danger of [illegible]

Treatment

In treating sprue it must be remembered that we are dealing with a disease of unknown etiology. The number and variety of sprue treat-

ments for which success has been claimed in the past are quite bewildering, and this raises a natural doubt of their real value. Among these are the milk cure administered with a teaspoon, the high carbohydrate diet, the high protein diet, the raw beef diet, the pure fruit diet, the strawberry diet, and the banana diet

The treatment prescribed must depend on the individual patient's symptoms. A severe case is in a state of starvation with symptoms due to multiple nutritional deficiencies of protein, fat, carbohydrate, minerals, vitamins, and hæmopoietic factors.

Liver.—This must take first place. Manson introduced liver for the treatment of sprue after discovering that pills of dried crow's liver were an ancient native remedy in China, and many years before extracts were produced for injection, liver by mouth—raw, lightly cooked, or in freshly-prepared soup—held a great reputation This reputation was enhanced by the work of Minot and Murphy on the effects of liver in pernicious anæmia, later the liquid extract given by mouth was also found effective Crude aqueous liver extract given parenterally is now recognized as the most specific remedy available, and should be given in large daily doses (4 to 8 c cm intramuscularly) When folic acid is available, it may be expected to give equally good results

Rhoads and Miller showed in 1934 that crude liver extract given parenterally controlled sprue, increasing absorption from the bowel. Under this treatment alone the mouth lesions heal and the intestinal symptoms improve, the stools becoming smaller, less frequent, and gradually more formed with a decrease in the fat content. There is gain in weight and rapid improvement in the blood picture Refined liver extracts may help the anæmia, though not so strikingly, but they lack the known and unknown factors in crude extracts which have such a dramatic effect upon the course of the disease

Campolon, Hepastab, Pernæmon Forte, Hepolon, and Plexan are examples of the crude extracts Daily injections should be continued for some two weeks and then reduced gradually as the patient's condition improves to 4 c cm at intervals of one or two weeks In some very severe cases they may have to be continued indefinitely.

Diet.—The principle of dieting in sprue is to attempt to reduce the distension and diarrhœa and to replace the deficiencies. The bowel distension is chiefly in the small intestine, which is dilated and loaded with digested but unabsorbed food, and the diarrhœa is due to the excessive amount of fat in the stools together with the other constituents which are normally absorbed from the small intestine.

In a severe case with soreness of the mouth, it is rational to start with two-hourly feeds of milk and to add solids as the symptoms subside Bed rest is just as important in sprue as in peptic ulcer (Keele and Bound) and should be insisted upon in the early stages. The average case can start with solid food. A high-protein, low-fat, and low-carbohydrate diet is generally employed, because this diminishes the steatorrhœa an fermentation. Eggs and underdone steaks are usually well tolerated bread is given in the form of thin toast or Ryvita. Sprulac, a dried mi

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with high protein and low fat and carbohydrate, is often better tolerated than fresh milk. Proteolysed liver in soup has proved valuable, and marmite or yeast may be included for possible therapeutic effects Added vitamins are indicated· nicotinic acid, riboflavin and ascorbic acid; also vitaminized oil in capsules when the fat of the diet is low, since fat-soluble vitamins may be deficient. When gastric acidity is low dilute hydrochloric acid should be given in lemon or orange drinks during meals. If there are signs of low blood calcium, calcium gluconate should be given intramuscularly. Much patience is required in treating sprue patients, and careful nursing is necessary with particular attention to the mouth. Gradually, as the symptoms subside, more carbohydrates and fats should be given and normal diet approached by trial. Some patients can ultimately resume ordinary food, but often it is found that some permanent restriction is necessary, particularly of fatty foods.

The diets which follow will be helpful in the treatment of severe cases: a case of average severity may begin at Stage 3.

Sprue diet

Stage 1 *P*.50, *F* 5, *C* 119 *Ratio* 1 0 1 2 3, *Cals*. 721

Hour

0730 Skimmed Milk, 8 ounces, flavoured with tea

0930 Marmite, 1-2 teaspoons in hot water, 10 ounces.

1230 Skimmed Milk, 8 ounces. One ripe banana

1400 Skimmed Milk, 8 ounces, with Marmite 1–2 teaspoons

1600 Skimmed Milk, 8 ounces, flavoured with tea

1800 Orange Juice, 8 ounces, sweetened with 1 ounce of Glucose.

000 Skimmed Milk, 8 ounces, with Marmite 1–2 teaspoons

2200 Skimmed Milk, 8 ounces.

Stage 2 *P* 110, *F* 17, *C* 160 *Ratio* 1 0 2 1 4 *Cals* 1,233

Hour

0730 Skimmed Milk, 10 ounces, flavoured with tea and sweetened with Glucose ½ ounce

0930 Marmite, 1–2 teaspoons in hot water, 10 ounces.

1100 Skimmed Milk, 10 ounces—may be served as cocoa

1230 Liver Soup, 8 ounces Fish minced, 4 ounces, with white sauce or Marmite gravy One slice of twice-baked bread (one ounce) One ripe banana

1400 Skimmed Milk, 10 ounces, with 1–2 teaspoons of Marmite

1600 Skimmed Milk, 10 ounces, flavoured with tea

1800 Orange Juice, 8 ounces, with Glucose one ounce. One r banana

2000 Skimmed Milk, 10 ounces, with 1–2 teaspoons of Marmite

2200 Skimmed Milk, 10 ounces.

*Stage 3 P.144, F 23, C.198. Ratio 1 . 0·2 : 1·4. Cals. 1,575

Hour

0730 Skimmed Milk, 10 ounces, flavoured with tea and ½ ounce sugar.

0930 Marmite, 1–2 teaspoons in hot water, 10 ounces.

1100 Skimmed Milk, 10 ounces—may be served as cocoa.

1230 Liver Soup, 8 ounces. Fish 4 ounces minced, served with white sauce. One thin slice of twice-baked bread (1 ounce). One banana.

1400 Skimmed Milk, 10 ounces, with 1–2 teaspoons of Marmite

1600 Skimmed Milk, 10 ounces, flavoured with tea. One banana.

1800 Chicken, 4 ounces or Liver, 4 ounces. Twice-baked bread (1 ounce) Orange Juice, 8 ounces, sweetened with sugar, 1 ounce.

2000 Skimmed Milk, 10 ounces, with 1–2 teaspoons of Marmite.

2200 Skimmed Milk, 10 ounces.

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* A case of average severity may begin with Stage 3.

Stage 4 *P*.168, *F*.69, *C* 235 *Ratio* 1 · 0 4 . 1 4. *Cals* 2,237

Hour

0730 Whole Milk, 5 ounces, in tea with sugar. One lightly-boiled egg One slice of twice-baked bread (1 ounce) Butter ½ ounce.

0930 Marmite, 1-2 teaspoons in hot water, 10 ounces

1100 Skimmed Milk, 10 ounces—may be served as cocoa.

1230 Liver Soup, 8 ounces Fish, 8 ounces, with white sauce One slice of twice-baked bread (1 ounce) Two bananas. 10 ounces of custard made with skimmed milk

1400 Skimmed Milk, 10 ounces, with 1-2 teaspoons of Marmite.

1600 Whole Milk, 5 ounces, in tea with sugar. One banana

1800 Chicken, 4 ounces, or Lean Meat, 4 ounces. One slice of twice-baked bread (1 ounce) Orange Juice, 8 ounces, sweetened with sugar, 1 ounce.

2000 Skimmed Milk, 10 ounces, with 1-2 teaspoons of Marmite

2200 Whole Milk, 10 ounces.

Stage 5 *P*.162, *F* 85, *C*.320. *Ratio* 1 . 0·5 . 2 0 *Cals*. 2,693

Hour

0730 One lightly-boiled egg Twice-baked bread (2 ounces) Butter ¼ ounce. Tea with 5 ounces of whole milk Sugar ½ ounce

0930 Marmite, 1–2 teaspoons in hot water, 10 ounces Biscuits, 2 ounces.

1100 Skimmed Milk, 10 ounces as cocoa.

1230 Liver Soup, 8 ounces Steamed Fish, 8 ounces, with white sauce Potato, 4 ounces. Two bananas. Custard with skimmed milk, 10 ounces.

1400 Whole Milk, 10 ounces, with 1–2 teaspoons of Marmite.

1600 One banana Tea with 5 ounces of whole milk Sugar, ½ ounce

1800 Lean Meat or Chicken, 4 ounces. Two slices of twice-baked bread (2 ounces). Butter, ¼ ounce. Orange Juice, 8 ounces, sweetened

2000 Whole Milk, 10 ounces, flavoured with Marmite.

2200 Whole Milk, 10 ounces.

Stage 6 *P*.174, *F*.115, *C*.343. *Ratio* 1 : 0 7 : 2 0. *Cals*. 3,120

Hour

0730 One ounce Porridge Oats as porridge, 8 ounces, with 10 ounces of whole milk. Two lightly-boiled eggs. ½ ounce marmalade. ½ ounce butter. Two slices twice-baked bread (2 ounces) Tea with 5 ounces whole milk. Sugar, ½ ounce.

1000 Marmite, 1–2 teaspoons in hot water, 10 ounces. Biscuits, 2 ounces.

1230 *Liver Soup, 8 ounces. Steamed Fish, 8 ounces, with white sauce.* Potato, 4 ounces. Light Steamed Pudding—one portion. Two bananas.

1400 Whole Milk, 10 ounces, with 1–2 teaspoons Marmite.

1600 Tea with 5 ounces whole milk with sugar, ½ ounce. One slice twice-baked bread (1 ounce). Butter, ½ ounce. One banana.

1800 Lean Meat or Chicken, 4 ounces. Two slices twice-baked bread (2 ounces). ½ ounce butter. One tomato. 8 ounces sweetened orange juice.

2200 10 ounces Whole Milk. Biscuits, 2 ounces.

Notes

1. *Until Stage 5 is reached, the patient should remain in bed.*

2. Only those items ordered on the diet sheet should be given and quantities stated should be strictly observed.

3. All cocoa and custard for sprue patients is to be made with skimmed milk. Custard is to be made with custard powder.

4. Tea in diets 1, 2, and 3 to be made with skimmed milk. Tea in diets 4, 5, and 6 to be made with whole milk.

5. When in good supply, liver may be substituted for chicken or lean meat.

6. Twice-baked bread. This is prepared by taking a slice of bread roughly 4½ inches square by ¼ inch thick and placing it in a hot oven until it is light brown in colour and chippy in consistency. *This should weigh one ounce after baking.*

Butter. A cube of butter with sides ¾ inch long, weighs approximately ¼ ounce. Another method of measuring is to take a 1 lb. packet and divide it into 64 equal portions.

7. A case of average severity may begin at Stage 3.

ORDER FOR SPRUE DIET (ORDER AS "NO DIET")

	Stage or Sprue Diet No					
	1	2	3	4	5	6
Milk, skimmed, pints	2½	3	3	2	1	—
Milk, whole, pints	—	—	—	1	2	1½
Oranges, number	2	2	2	2	2	2
Bananas, number	1	2	2	3	3	3
Glucose or cane sugar, ounces	1	1	1½	2	2	2
Marmite, ounces	½	½	½	½	½	½
Bread, ounces	—	1½	3	4	6	6
Liver, as raw, ounces	—	8	8	8	8	8
Fish, as raw, ounces	—	8	8	16	16	16
Chicken, as raw, ounces	—	—	10	10	10	10
OR						
Lean Meat, as raw, ounces	—	—	8	8	8	8
Flour as white sauce, ounces	—	½	½	½	½	½
Cocoa, ounces	—	½	½	½	½	½
Tea, ounces	—	⅓	⅓	⅓	⅓	⅓
Butter, ounces	—	—	—	¼	½	1½
Eggs	—	—	—	1	1	2
Biscuits, ounces	—	—	—	—	2	4
Potato, as raw, ounces	—	—	—	—	8	8
Marmalade	—	—	—	—	—	½
Tomato	—	—	—	—	—	1
Porridge Oats, ounces	—	—	—	—	—	1
Steamed pudding as below—						
Butter, ounces	—	—	—	—	—	⅓
Flour, ounces	—	—	—	—	—	2-3
Eggs	—	—	—	—	—	⅓
Sugar, ounces	—	—	—	—	—	¼

NOTES

1. Sugar—in diets 1 and 2 is best given as Glucose.

2. Chicken and lean meat—in diets 3, 4, 5, and 6. To ensure variety, one or the other should be ordered, not both on the same day.

3. Diet 3—when Liver is in good supply this should be ordered in place of lean meat, *i.e.*, on every second day alternatively with chicken.

4. "Vegemite" may be substituted for Marmite.

5. Sprue diets must be ordered strictly in accordance with the above tables. Extras are not allowed and increase in quantity is not permitted.

SULPHONAMIDE DRUGS

The sulphonamide drugs have an important place in the treatment of a number of tropical and sub-tropical diseases. Certain principles govern their use—the first, that the infecting organism must be sensitive to the preparation employed. It is essential, therefore, to know the range of activity and potency of the various sulphonamides available, and to correlate this with the elementary facts of their pharmacology. For fuller details the reader may consult the Medical Research Council's *War Memorandum No. 10—The Medical Use of Sulphonamides*, 1945, Second Edition. (H.M S.O. London 1s. 3d.).

General Purposes.—Five sulphonamides are in common use for general [illegible] *sulphathiazole*, sul- [illegible] is more generally [illegible] "sulphamethazine". In this article it will be referred to as sulphamezathine. It is a chemical homologue of sulphadiazine. Sulphanilamide is effective against the beta-hæmolytic streptococcus, meningococcus, gonococcus, *Bact. coli*, and, to some extent, *Ps. pyocyanea*, *Cl. welchii*, *H. ducreyi*, and *Past. pestis*, but it is not active enough for clinical use against infections with *Staphylococcus aureus* and pneumococci. The other four sulphonamides named are more active against the same organisms as sulphanilamide, and are also active enough for use against staphylococci and pneumococci. The four preparations are about equally potent against pneumococci; against staphylococci, sulphapyridine is definitely inferior to the other three. With the exception of lymphogranuloma inguinale and possibly trachoma, virus diseases do not respond to sulphonamides; though secondary infection may be successfully controlled. The effect on *Streptococcus viridans* infections is usually negligible. Choice of sulphonamide is frequently limited by availability. *Sulphathiazole*, *sulphadiazine*, or sulphamezathine are to be preferred to sulphapyridine on [illegible] unpleasant reactions are [illegible]

Urinary Infections.—The kidney has a power of fifty-fold concentration. An effective strength of a sulphonamide drug in the urine can therefore be achieved with a relatively small concentration in the blood. For choice, the best preparations are those which do not form insoluble acetylated crystals, these include sulphanilamide, sulphamezathine, and sulphacetamide (trade name: "Albucid").

Intestinal Infections.—The best results (clinical and bacteriological cure) are obtained with drugs which are not readily absorbed from the bowel and are at the same time active against intestinal pathogens. Sulphaguanidine and succinyl sulphathiazole ("Sulphasuxidine") fulfil these criteria and are the drugs of choice in bacillary dysentery, sonne-dysentery infections are said to respond better to succinyl sulphathiazole and sulphadiazine than to sulphaguanidine. In the absence of sulphaguanidine or succinyl sulphathiazole, it has been found that most cases of bacillary dysentery respond well to treatment with sulphapyridine, sulphathiazole, or sulphadiazine The sulphonamide group is ineffective in enteric fever and bacterial food poisoning. Although their value in cholera is still uncertain, it seems worth proceeding as in bacillary dysentery.*

Local Applications.—The first essential is that the drug should be soluble in a serous exudate. This rules out sulphapyridine, which merely forms an insoluble cake, whereas the highly-soluble sulphanilamide is eminently suitable The most widely-used preparations are either sulphathiazole or a mixture of sulphanilamide (3 parts) and sulphathiazole (1 part). Applications may be made as a fine powder, as a 20 per cent. microcrystalline suspension, or as a 5 per cent. water-miscible cream. Sulphacetamide (albucid), on account of its non-irritating properties, is particularly suitable for local application to the conjunctival sac. Pus does not inhibit the action of "marfanil" and related preparations, these can be used only for local application.

Route of Administration.—Sulphonamide drugs may be administered parenterally or by the mouth. They should always be given by mouth except for fulminating infections, because an immediate effect is imperative, in unconscious patients, because swallowing is impossible, and if for any other reason such as vomiting, oral difficulties, or gastro-intestinal disorders, the ingestion and absorption of the drug is likely to be difficult or irregular. In all these circumstances give sulphonamide parenterally, but remember that oral administration should replace parenteral injection as soon as circumstances permit. The preparations available for parenteral injection are the soluble sodium salts of sulphapyridine, sulphathiazole, and sulphadiazine. These are highly alkaline solutions dispensed in amounts of 3 0 c.cm. containing 1 0 g. of the drug, they must be diluted to at least 10 c.cm. before being injected intravenously. Intramuscular injection should be avoided on account of the high incidence of necrosis of muscle. Intrathecal injection is prohibited Sulphanilamide is sufficiently soluble to be made up as

* Phthalyl sulphathiazole, a new compound, is said to be a more substitute for succinyl sulphathiazole.

saturated solution in saline (0·8 per cent.) and administered by intravenous drip or even per rectum. The sodium salts mentioned above can also be incorporated in a saline drip.

Dosage.—The guiding principle is to secure and maintain an effective blood-stream, spinal-fluid, or local concentration, and with serious generalized infections it is essential that the administrations should be made night and day; otherwise the concentration during the night hours may sink below an effective level. In the bloodstream, an effective level is from 5–10 mg. per cent; in the spinal fluid from 3–5 mg. per cent. This should be checked in cases of apparent failure. With a sensitive organism a clinical effect should be obtained, usually in less than seven days, or at most ten days. If no such effect is apparent, the inference is that the infecting organism is insensitive or the preparation in use is not

... somewhat on ... In

routine at four-hourly intervals; the pharmacological properties of sulphadiazine permit six-hourly intervals. The table shows the average effective dosage for an adult of about 10 stone. Children, weight for ... the tolerance of adults; in infants it is as much ... lcu- ... y to give a large "loading" dose, followed by regular ... oses

citrate with each dose of sulphonamide. ...

above fluid intake and urinary output with all sulphonamides.

Type of Infection	*Loading Dose*	*Maintenance Dose*
Acute . .	2–4 g. intravenously 1·5 g. by mouth.	1·5–2 g. four hourly for 6–7 days.
Moderate ..	2–3 g. by mouth.	1 g. four hourly for 6–7 days.
Mild ..	1–2 g. by mouth.	0 5 g. four hourly for 6–7 days.

For *urinary infections* the dosage prescribed for moderate infections may be used, followed if necessary by a second course after a four-day interval. In persistent cases, the administration of 0.5 g. sulphamezathine twice daily over a prolonged period is sometimes useful.

For *intestinal infections* the usual adult dose of sulphaguanidine or succinyl sulphathiazole is 3 g. four times daily for three days, followed by 3 g. twice daily for four days, for severe infections the dose may be increased to 5 g. Fairley and Boyd's scheme is given on p. 115. Over-dosage, or too long-continued dosage, with sulphaguanidine or succinyl sulphathiazole can upset vitamin synthesis by intestinal bacteria. Treatment should not, therefore, be prolonged beyond the limits prescribed.

For *local* (*topical*) use, 5–10 g. is the most that may be applied to serous cavities, but up to 15 g. may be used with muscle wounds or lesions of skin.

It should be borne in mind that the application of 1.0 g. to tissue gives rise to a concentration of from 0.5 to 1.0 mg. per cent in the blood in from 6 to 12 hours' time, simultaneous oral administration should be adjusted to allow for the anticipated absorption. Skin lesions should not have local applications for a period exceeding five days because of the risk of sensitization.

Complications.—*Cyanosis* frequently occurs, it may be due to methæmoglobin or sulphæmoglobin, but it has no material importance except in anæmic patients and in the need to differentiate it from cyanosis due to cardiac insufficiency, especially in respiratory infections. Exclusion of sulphur-containing foods and drugs is no longer considered necessary, but saline and drastic purgatives which cause distension of the bowel should be avoided.

Vomiting is most common with *sulphapyridine*, but it may occur with any sulphonamide. Administration of the sulphonamide along with alkali (sodium bicarbonate and sodium citrate, grains 20 of each) or in mucilage of tragacanth or milk is sometimes helpful, but one of the best measures is to divide the total four-hourly dose into four portions and administer one portion each hour; this is frequently effective in the early stages of a severe illness, and this is when vomiting is most prominent.

Agranulocytosis is a serious complication. It should be appreciated that some degree of neutropenia is extremely common whenever sulphonamide drugs are exhibited, but serious and fatal agranulocytosis is rare. The dangerous state may be regarded as having been approached if the *polymorphonuclear count* falls below 2,000 per c mm., especially if this reduction is associated with lassitude, headache, and evidence of toxæmia. It may be regarded as being established when the *polymorphonuclear count* falls below 1,000 per c mm. The complication arises most commonly from the fifth to seventh days. If it has happened once it usually recurs if a second course *is* administered. In certain circumstances, a difficult decision may be required whether *to* risk agranulocytosis in face of a disease that will probably be fatal unless sulphonamide treatment is given. The treatment of agranulocytosis is to [illegible] the drug

saturated solution in saline (0·8 per cent) and administered by intravenous drip or even per rectum. The sodium salts mentioned above can also be incorporated in a saline drip.

Dosage.—The guiding principle is to secure and maintain an effective blood-stream, spinal-fluid, or local concentration, and with serious generalized infections it is essential that the administrations should be made night and day, otherwise the concentration during the night hours may sink below an effective level. In the bloodstream, an effective level is from 5–10 mg. per cent.; in the spinal fluid from 3-5 mg. per cent. This should be checked in cases of apparent failure. With a sensitive organism a clinical effect should be obtained, usually in less than seven days, or at most ten days. If no such effect is apparent, the inference is that the infecting organism is insensitive or the preparation in use is not active enough. If further chemotherapy is contemplated, the preparation should be changed, an early bacteriological examination is a useful check against useless treatment. Almost as the converse of these principles it may be said that too early omission of the drug, especially in dangerous generalized infections, is apt to permit a relapse or an exacerbation In spite of favourable and dramatic effects, as in pneumonia, almost full doses should be continued for some 48 hours after the desired clinical result has been produced. Pus inhibits the action of sulphonamide drugs (except "marfanil", which is for local use only), and no effect should be looked for so long as a closed suppurating focus is present.

The sulphonamide drugs (except sulphadiazine) are administered as a routine at four-hourly intervals; the pharmacological properties of sulphadiazine permit six-hourly intervals. The table shows the average effective dosage for an adult of about 10 stone. Children, weight for weight, have about twice the tolerance of adults; in infants, it is as much as threefold—these considerations should be borne in mind when calculating the dose for children and infants. In all cases, it is customary to give a large "loading" dose, followed by regular maintenance doses. With all the usual sulphonamides except sulphanilamide, sulphacetamide, and probably sulphamezathine, it is essential to ensure an adequate flu d intake (3 5 litres—6 pints—per 24 hours) and urinary output (1·5 litres—
[illegible]

Type of Infection		*Loading Dose*	*Maintenance Dose*
Acute ..	..	2–4 g. intravenously 1·5 g. by mouth.	1·5-2 g. four hourly for 6-7 days.
Moderate	..	2–3 g. by mouth.	1 g. four hourly for 6-7 days.
Mild	.	1–2 g. by mouth.	0 5 g. four hourly for 6-7 days.

For *urinary infections* the dosage prescribed for moderate infections may be used, followed if necessary by a second course after a four-day interval. In persistent cases, the administration of 0 5 g. sulphamezathine twice daily over a prolonged period is sometimes useful.

For *intestinal infections* the usual adult dose of sulphaguanidine or succinyl sulphathiazole is 3 g four times daily for three days, followed by 3 g twice daily for four days; for severe infections the dose may be increased to 5 g Fairley and Boyd's scheme is given on p 115 Over-dosage, or too long-continued dosage, with sulphaguanidine or succinyl sulphathiazole can upset vitamin synthesis by intestinal bacteria Treatment should not, therefore, be prolonged beyond the limits prescribed.

For *local* (*topical*) use, 5–10 g is the most that may be applied to serous cavities, but up to 15 g. may be used with muscle wounds or lesions of skin.

It should be borne in mind that the application of 1 0 g to tissue gives rise to a concentration of from 0 5 to 1 0 mg per cent. in the blood in from 6 to 12 hours' time, simultaneous oral administration should be adjusted to allow for the anticipated absorption. Skin lesions should not have local applications for a period exceeding five days because of the risk of sensitization.

Complications—*Cyanosis* frequently occurs, it may be due to methæmoglobin or sulphæmoglobin, but it has no material importance except in anæmic patients and in the need to differentiate it from cyanosis due to cardiac insufficiency, especially in respiratory infections Exclusion of sulphur-containing foods and drugs is no longer considered necessary, but saline and drastic purgatives which cause distension of the bowel should be avoided.

Vomiting is most common with sulphapyridine, but it may occur with any sulphonamide. Administration of the sulphonamide along with alkali (sodium bicarbonate and sodium citrate, grains 20 of each) or in mucilage of tragacanth or milk is sometimes helpful, but one of the best measures is to divide the total four-hourly dose into four portions and administer one portion each hour, this is frequently effective in the early stages of a severe illness, and this is when vomiting is most prominent.

Agranulocytosis is a serious complication. It should be appreciated that some degree of neutropenia is extremely common whenever sulphonamide drugs are exhibited, but serious and fatal agranulocytosis is rare. The dangerous state may be regarded as having been approached if the *polymorphonuclear count* falls below 2,000 per c cmm, especially if this reduction is associated with lassitude, headache, and evidence of toxæmia. It may be regarded as being established when the *polymorphonuclear count* falls below 1,000 per c mm. The complication arises most commonly from the fifth to seventh days If it has happened once it usually recurs if a second course is administered In certain circumstances, a difficult decision may be required whether to risk agranulocytosis in face of a disease that will probably be fatal unless sulphonamide treatment is given. The treatment of agranulocytosis is to stop the drug

at once, force fluid intake in order to ensure elimination, and transfuse, repeatedly, if necessary with fresh blood. Pyridoxine (vitamin B_6) may apparently cause dramatic improvement.

Hæmolytic Anæmia.—This rare complication arises from the second to sixth days, and is more common in children than adults, especially when sulphanilamide is used. The treatment is to stop the drug, force fluids, and give a fresh blood transfusion if necessary.

Drug-Fever.—This is usually accompanied by a rash, but if not it is difficult to differentiate from an exacerbation of the original infection. The treatment is to stop the drug and force fluids.

Skin manifestations.—Erythema, dermatitis, and light-sensitivity may be caused by general administration of sulphonamides, but are most often the result of local applications continued beyond a period of five days. The treatment is to stop the drug and give copious fluids. A skin rash may herald further complications; its appearance should always call for a leucocyte count. Skin sensitivity may endure for years and may be precipitated again by oral administration.

Sensitization.—Some of the "toxic" reactions are possibly due to sensitization. This may not have developed for all preparations; therefore the first step, if sensitivity is diagnosed, is to make a trial with a different compound. Desensitization to sulphonamide drugs may also be attempted on orthodox lines, using minute doses (0·1 g.) at four-hourly intervals. The results may not be very successful; if so, the attempt should be given up.

Urinary Tract Complications.—Crystalline deposits of sulphapyridine, sulphathiazole, and sulphadiazine or their acetyl derivatives are insoluble in a concentrated and acid urine and may give rise to hæmaturia (microscopic or macroscopic), calculus formation, and obstructional anuria. This complication is a very real danger in a dehydrated subject, especially in a tropical climate. An adequate urinary output is more important than reaction, and trouble rarely arises if the output is maintained at 1·5 litres (50 fl. oz.) each 24 hours. Nevertheless, it is a good precaution to keep the urine alkaline to litmus by giving alkali (*see* above) with each dose of sulphonamide. If the first urine passed on any given morning is found to contain crystals, alkali should be begun at once.

TROPICAL EOSINOPHILIA

In the tropics, many develop moderate degrees of eosinophilia; indeed an eosinophil count of from 4 to 8 per cent. may be considered within normal limits for those long domiciled in hot countries. Such counts are often caused by long standing, low-grade helminth infestation; higher counts are associated with declared infestations.

From tropical and sub-tropical countries, there have come many reports of a form of *asthma* associated with a high degree of eosinophilia. As far as is known, it is not caused by helminths. Mites have been found in the sputum in one small series in Ceylon but only after prolonged search

and the use of special concentration methods Confirmation of this important observation is still lacking from other sources.

The syndrome was described by Weingarten in India among Indians, in recent years, cases have also been noted among Europeans in many widely-separated parts of the Far East and Middle East.

Tropical eosinophilia may be insidious in onset and chronic from the start, or there may be an initial febrile attack with slight splenomegaly Asthmatic attacks which may be severe and resistant to ordinary anti-spasmodic therapy are a feature of the established disease Debility with loss of weight, anorexia, and persistent cough have often suggested a serious underlying illness, and it is not surprising that pulmonary tuberculosis has been wrongly diagnosed in many cases Physical signs in the chest are usually minimal, being those of chronic bronchitis X-ray appearances in the lung fields are inconstant In many, probably a majority, the lung appearances are more or less normal, in others the lungs present a uniform mottling which is said to be highly characteristic when present Leucocytosis with eosinophilia, which is usually marked, is the most characteristic and diagnostic feature The leucocyte count usually lies between 20,000 and 60,000 per c mm with 20 to 60 per cent eosinophils

A most important and encouraging peculiarity of the disease is its ready response to arsenical medication Weingarten treated his cases with a course of six intravenous injections of neoarsphenamine first dose 0 15 g; second dose 0 3 g, subsequent doses 0 45 g., three days' interval between doses Good results have recently been reported from the use of other arsenicals, including mapharside given parenterally and carbarsone or stovarsol by mouth.

The effect of the arsenic on both the clinical condition and on the blood picture has usually been dramatic and apparently lasting, although there may be an initial aggravation of the symptoms and of the eosinophilia The lung mottling shown by X-rays may take a considerable time to disappear, although the clinical picture as a whole shows rapid improvement.

TYPHOID FEVER

Thanks to protective inoculation and efficient sanitary precautions, typhoid fever is no longer one of the chief disease factors among our armies in the field As the closely-allied paratyphoid fever is dealt with at some length, it is not necessary to describe fully so well-known a malady as typhoid fever

These Memoranda will consider only such points concerning typhoid in the tropics as appear to be worthy of special attention, and in the first place it may be said that in hot countries the attack tends to be more severe and prolonged than in temperate climates (Fig 75) As a result the mortality is often higher in the tropics and death may ensue as early as the sixth day of disease in the hypertoxic form Degeneration of the myocardium is common and myocarditis frequently brings about a fatal issue

In the second place the medical officer should know that unprotected

men of indigenous races, whether Indian or African, are not immune from enteric infection. Enlisted troops undergo inoculation and so usually escape, but camp followers are sometimes uninoculated and so may suffer. At the same time they are much more liable to dysentery than to enteric, and it is quiet possible that many possess an acquired immunity, having suffered in childhood. It is interesting to note that, in India, Gurkhas have been found to be among those most liable to infection.

Young adult Europeans, recently arrived in the tropics or sub-tropics, are specially liable to infection. This is largely due to the newcomer not yet having fully undergone that complicated and indefinite but very real process known as "acclimatization"; an important item in this faulty adaptation is ignorance of how to avoid, by simple hygienic precautions, the special dangers inherent in hot climates. The chances of infection are much greater in the tropics, partly owing to the prevalence of fly vectors; over-fatigue, over-exertion, and exposure to the debilitating effects of the tropical heat also act as predisposing causes.

Constipation rather than diarrhœa is the rule in tropical typhoid, and the exanthem is often absent or difficult to differentiate from the varied assortment of spots and pimples found constantly on the bodies of most residents in hot climates.

It is well to remember that when typhoid attacks a patient with malaria, the enteric onset may be very sharp and sudden and associated with rigor. The temperature, however, soon becomes continuous. Often the curve fails to follow the typical course of typhoid, so well known to the medical student.

The rise is usually abrupt even in non-malarial cases and is generally followed by a "high continued fever" which keeps steadily above 101° F. and for a long time does not vary more than 2° F. Towards the end of the third week it may swing a little and then descend by lysis. Another and severe type is the "continuo-remittent" where the temperature keeps up but shows a greater amplitude, producing a more spiked tracing on the chart (Fig. 75). Yet another remittent form closely simulates sub-tertian malaria (*see* p. 179).

Short abortive attacks are met with where the fever lasts only a few days. These may readily be missed in the absence of routine systematic blood cultures and agglutination tests, and missed, too, in spite of these aids to diagnosis.

In non-European races, whether African, Arab, or Indian, the disease conforms closely to the type met with in Europeans. Perhaps the slow pulse is its most characteristic feature. The old idea that there was a hybrid disease "typho-malaria" has been exploded. The two diseases not infrequently occur at the same time in the same patient and may modify each other in various directions. The help of the laboratory is usually required for the diagnosis of such a mixed infection. A rare chronic form of enteric fever sometimes lasting as long as a year is now a recognized entity.

Cases which show little variation in the range of temperature, which runs steadily along a line in the neighbourhood of 103° F. or 104° F.,

Fig. 75.

[Temperature chart, No. 3: days of disease 2–13, morning/evening temperatures 97°–106° F (35°–42° Centigrade), pulse, respiration and bowels rows; "Died" written on day 13.]

Severe Typhoid with High Remittent Pyrexia terminating fatally on thirteenth day Tyhoid Bacilli cultivated from finger blood on tenth day —Rogers, "Fevers in the Tropics"

for day after day and even week after week showing little or no amplitude even in a four-hourly chart, are liable to be specially dangerous and have a tendency to a fatal termination.

Diagnosis.—The diagnosis of typhoid fever, especially in the British soldier, is apt to be a complicated problem. This is largely due to the fact that, because of previous T.A.B. *inoculation*, no reliance can be placed on the result of the Widal reaction. It must be remembered that cases of undoubted typhoid fever may show no significant rise in specific agglutinins throughout the illness.

The only certain test is the isolation of *B. typhosus* on culture from the blood, which can usually be effected, if proper precautions are taken, during the first week or ten days of a moderate or severe attack of the typhoid group. But blood cultures remain positive for a considerably longer period, and are often positive during a relapse. After fifteen days or so of fever positive cultures are more likely to be obtained from the fæces or, less commonly, from the urine, and daily specimens of both fæces and urine should be sent to the laboratory for this purpose. It should be noted that the presence of *B. typhosus* in the stools or urine [illegible]

[illegible] ally suggests typhoid fever, the presence of *B. typhosus* in any of the secretions or discharges clinches the diagnosis. Total and differential white blood counts are of the greatest value in the differential diagnosis of fevers of the tropics and should never be omitted.

The detection of the carrier state may be helped by Felix's Vi-agglutination test.

Recently, the epidemilogical investigation of outbreaks of typhoid fever has been much assisted by the use of bacteriophage for typing virulent [illegible]

[illegible] events leading up to spread of the infection.

Differential Diagnosis.—As already stated, malaria is the disease most difficult to distinguish from typhoid in the tropics when resort is had to clinical examination alone. Both diseases may exhibit chills, continued fever, bronchitis, enlarged spleen, tenderness and gurgling in the right [illegible] Herpes [illegible]

The enlarged spleen of typhoid fever is usually much more difficult to palpate than that of malaria. This elusive character of the typhoid spleen is partly due to the generalized abdominal distension and tenderness common to all enteric-group infections, but the organ is also usually much softer than in malaria, it may indeed be almost diffluent in hypertoxic cases.

In typhoid fever the abdominal tenderness is usually generalized and is often accompanied by gurgling in the right iliac fossa; in malaria,

... tenderness as there may be is usually limited to the splenic area.

The differential diagnosis from paratyphoid A, B, or C can be made only by bacteriological methods, although each of the paratyphoid fevers has its own clinical characteristics (see paratyphoid fever, p 215). these are not sufficiently distinct or constant to enable a firm diagnosis to be made on clinical grounds alone The same is true of infections with *B fæcalis alkaligenes* and some members of the salmonella group

Visceral leishmaniasis (kala-azar) may closely mimic a prolonged enteric-group infection and this possibility should always be borne in mind if the patient has visited an area where kala-azar is endemic

If accompanied by jaundice, as it may well be, typhoid fever has to be distinguished from Weil's disease and, occasionally, from infective hepatitis

The rash and clinical course of typhus may closely resemble those of typhoid fever It should be remembered that the two diseases were clearly separated only after the introduction of exact bacteriological methods.

Among a host of other diseases to be distinguished, the following may be mentioned undulant fever, infective endocarditis, generalized tuberculosis, tuberculous peritonitis, pneumonia—especially of the central nonsymptomatic type, psittacosis, and septicæmia

During the 1939–45 war a close connection between enteric-group infections and dysentery has been noteworthy in some theatres In the Middle East typhoid or paratyphoid bacilli were cultured from the stools of many patients suffering from clinical dysentery with or without fever In one considerable series, 26 8 per cent of cases of enteric-group infections which came to autopsy were found to have typhoid ulcers in the large bowel In a majority of the cases, these ulcers did not extend beyond the cæcum or proximal half of the ascending colon, but in a few, typhoid ulcers were to be seen scattered throughout the whole of the large gut from cæcum to rectum In a few cases there may have been active, double infection with *B typhosus* and *B dysenteriæ*, but in the majority the ulcers were typically of typhoid type and *B. typhosus* was cultured from them in several instances Severe toxic cases of typhoid fever may present such meningeal symptoms as stiff neck, double kernig, and uncontrollable headache A lumbar puncture may be necessary to differentiate these from true cases of meningitis

Finally, the abortive type of typhoid fever with pyrexia lasting only a few days and accompanied by little constitutional disturbance may be impossible to differentiate clinically from other short-term fevers such as sandfly fever, dengue, influenza, and the like Many a confident diagnosis of "clinical malaria" or "sandfly fever" has had to be changed on receiving the result of a blood culture

Prophylaxis.—Typhoid and paratyphoid fevers are spread by anything contaminated by the urine, fæces, or infected discharges of patients and carriers so that the strictest attention must be paid to cleanliness and the rapid disinfection of all excreta, discharges, utensils, bedding, clothing, and other articles soiled by patients or their excreta. The organisms are frequently conveyed by the hands, which should always be washed,

therefore, before meals or before handling food or water, special attention being paid to the finger nails.

All water should be regarded as suspect and should be purified before being used for drinking or cooking; this precaution should also be extended to aerated waters, and the sale of these and other drinks from unauthorized sources should be forbidden.

be put in

water, and special precautions should be taken against the adulteration of milk with polluted water. In the tropics all milk should be boiled or pasteurized under rigid supervision.

Anti-fly measures should be carried out and special steps taken to prevent the access of flies to excreta and food Conservancy measures must include the rapid and complete disposal of all excreta in such a way that water and food are not contaminated. (*See* Arthropod Pests and Appendix I)

In hot countries, vegetables, especially lettuces, are a source of danger and should not be eaten uncooked, only fruit which can be skinned, such as oranges or bananas, should be eaten raw Oysters and other shell fish may be contaminated with sewage and should be avoided unless they come from beds known to be unpolluted.

Cookhouse sanitation and the cleanliness of cooks must be of the highest standard, and no person who has suffered from any of the enteric-group fevers should be employed in the preparation or handling of food or on water duties.

All persons engaged in the handling of food and drink, or of utensils used in connection with these, must be medically examined. Ideally, their stools and urine should be bacteriologically examined before employment in order to exclude carriers Unfortunately, this is not always practicable.

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time. Inoculation gives protection for one year. To ensure the greatest possible degree of protection, inoculations should be carried out at least

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Treatment.—Unfortunately, no effective treatment of typhoid fever has yet been evolved.

feature of severe infections. Unfortunately, neither of these has any real effect on the course of the disease or on the mortality rate.

At present, then, the sulphonamides and penicillin would appear to

have their chief use in the treatment of septic complications or sequelæ caused by sulphonamide-sensitive or penicillin-sensitive organisms. With increasing purity and potency of penicillin there is hope that typhoid bacilli may yet fall within its effective range of action.

In the absence of effective specific therapy, skilled, meticulous, and unremitting nursing by an experienced nursing staff becomes all-important. But a warning note must be sounded, it is highly undesirable, even to obtain better nursing, to transport a patient with typhoid fever for long distances by road or rail except in the very early days of his infection. More than one catastrophe has resulted from misguided transportation of typhoid patients

The patient severely ill with typhoid fever may lie, little better than helpless, for weeks on end, therefore his mouth and skin need meticulous and constant attention and every resource known to a good nurse should be exploited to prevent bedsores. Urinary or fæcal incontinence, or both, may occur at any time—often when least expected, the bedclothes thus soiled need immediate changing The appetite is often poor and capricious, and every effort should be made to provide as varied and attractive a dietary as possible The services of a skilled dietitian should be enlisted if one is available Close attention should be paid to fluid intake and fluid balance to prevent dehydration on the one hand and "waterlogging" —an unlikely contingency—on the other

It is now generally recognized that the semi-starvation, and completely-fluid diet—almost universally adopted for typhoid patients in former times—is by no means the safeguard against hæmorrhage and perforation that it was once supposed to be Modern experience proves that patients do better on a nutritious, moderately-high-calorie, but non-roughage diet. The danger of perforation or hæmorrhage is no greater with the more liberal diet, and the incidence of such unpleasant sequelæ as exhaustion-psychosis and peripheral neuritis is thereby much diminished.

[illegible] has bet[illegible] 2,000 and 3,500 calories [illegible] such readily-digestible dishes as eggs, junket, mashed potatoes, apple sauce, chocolate, and so forth. Chocolate, which should, of course, be free from nuts or fruit, is valuable because it contains carbohydrate in a readily assimilable form and gives the chewing apparatus something to work on. Fruit drops, especially acid drops, are useful since they promote the flow of saliva and help to keep the mouth clean, they should be given, *of course, only to fully conscious and alert patients*

Marked abdominal distension and tympanites are important danger signals. It is true that their incidence is lessened rather than increased by a semi-solid, instead of a completely-fluid diet, none the less, their onset warns that, for a time at least, the diet must be drastically cut down and all items eliminated such as whole milk and excess of carbohydrate because these are liable to cause fermentation in the small intestine. Peptonized or skim milk may often be substituted with advantage. A flatus tube left in position for 20 minutes or more may

relieve the distension, a soap-and-water enema containing a few drops of turpentine is also a proved remedy. If these fail to relieve the distension a 0·5 c.cm injection of pituitrin or the comparable dose of some similar preparation may be tried; although this is not entirely without danger of causing perforation or hæmorrhage. One of the often-avoidable complications of the later weeks of typhoid fever is venous thrombosis, usually femoral. Every effort should be made to avoid this by preventing pressure on superficial veins. Passive, later active, movements of the limbs with skilled massage, by assisting the venous circulation, will help to prevent thrombosis and will also diminish the risk of post-typhoid neuritis.

For severe and prolonged cases the usual precautions should be taken to prevent foot drop.

The treatment of hæmorrhage, perforation, and other complications is fully dealt with in standard text-books and will not be discussed here.

UNDULANT FEVER

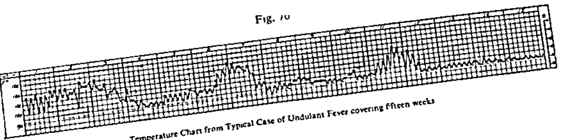
This long-continued fever is commonly known as Malta Fever, and has also been termed Mediterranean Fever and Gastric Remittent Fever among other titles. It has a wide geographical distribution throughout the Mediterranean littoral and is known to occur in Nigeria, Uganda, and Southern Africa, as well as in India, China, Hong Kong, the West Indies, etc The distribution is probably even more extensive than is realized at present, for the disease is readily confused with others if the possibility of its occurrence is not borne in mind, and the disease may now be regarded as cosmopolitan.

During recent years undulant fever due to the organism of contagious abortion (*Brucella abortus*) has been found to be widespread in Europe, America, and elsewhere.

Etiology.—The cause of the classical form of undulant fever is *Brucella melitensis*. These minute cocci or cocco-bacilli are found in the blood and give rise to an acute or chronic septicæmia. Goats are apt to harbour the organism and excrete it in their milk, so much so that the drinking of goats' milk is the principal method of acquiring the disease. As in typhoid, food, fingers, and flies are all probably operative in spreading infection, for, apart from milk, its products, such as cream and cheese, *may harbour the organism; surface soil and dust may become contaminated from the urine of human beings, goats, and other ruminants suffering from the disease and so lead to food infection; carrier* cases doubtless play a part; and flies may acquire the micrococcus from the urine or fæces Infection can take place through the skin and mucous membranes. The urine of ambulant human cases is, in all probability, a special source of danger. At the same time these additional methods of conveyance of the disease cannot bulk very largely or there would certainly have been many more cases during the 1914–18 war.

Brucella abortus and *Br. suis*, the causative organisms of contagious abortion of cows and pigs, also give rise to undulant fever in man. Such

Fig. 10



Temperature Chart from Typical Case of Undulant Fever covering fifteen weeks

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UNDULANT FEVER

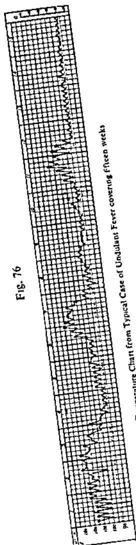
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Fig. 76



Temperature Chart from Typical Case of Undulant Fever covering fifteen weeks

infections cannot be differentiated clinically though, on the whole the organism of contagious abortion gives rise to a milder attack.

Symptoms.—Incubation period of six days to three weeks, usually fifteen days, followed by headache, insomnia, malaise, and anorexia. Constipation is the rule, and there is early splenomegaly and tenderness over the spleen. The temperature, of a remittent type, gradually rises, strongly suggesting the onset of typhoid. There may be epistaxis; slight bronchitis and cough with profuse sweats are not infrequent. The [illegible]

for three or four days by a step-like ascent the temperature falls by a similar descent and reaches normal on or about the tenth day.

The symptoms abate, the patient feels better for a few days, but the night sweats and *the emaciation, which sets in early, continue and then* the first of a long series of relapses manifests itself (*see* Fig. 76).

During these relapses the joint troubles arise, one joint usually being involved. There is no redness, but the part is swollen and there is effusion with severe pain. The condition is transient, lasting a few days but too often reappearing in another articulation The order of frequency, according to Hughes, is the hip, knee, shoulder, ankle, wrist, fingers, toes, elbow, intervertebral joints.

At the same time neuralgic pains set in, the peripheral nerves being specially affected and the sciatic often involved.

Albuminuria may be present and orchitis occasionally occurs as a late symptom. One testicle, only, is normally involved and complete recovery is the rule.

The febrile waves follow each other at short intervals and the disease runs its wearisome average course of sixty to seventy days, which may, however, extend to nearly a year. Naturally the patient becomes anæmic, he suffers from palpitation, his pulse is rapid and irregular. Mental depression lays hold of him, and it is important to remember that he may become a victim of the morphine habit. The total white count may be within normal limits or, more often, there is a moderate leucopenia (4,000 W B Cs per c mm) with a relative lymphocytosis.

While this is the usual undulatory fever the disease may be ambulant in type, or there may be an intermittent form running a mild course, or the attack may be malignant with a high continued fever, pulmonary complications, and a tendency to hyperpyrexia. The undulating type of fever is the most common, the febrile waves varying from ten days to six weeks. Intermissions of normal temperature usually last from seven to twelve days, but may be as long as a month. The temperature usually climbs and falls by step-ladder graduations, but the rise and fall may be *abrupt*.

When the undulating character is present the recurring waves usually become progressively shorter with increasing intermissions.

The severity of the disease cannot be gauged by a perusal of the temperature chart alone. The duration of the pyrexia is usually two to three months, but may vary within wide limits, up to two years.

The intermittent form is apt to be puzzling, as the morning temperature may be normal or sub-normal and the evening rise slight. Except in the malignant form the ultimate prognosis as regards life is good, only about 2 or 3 per cent. of the cases ending fatally.

Complications.—Arthritis, phlebitis, orchitis, neuralgia, and hæmorrhagic manifestations may be mentioned. Pulmonary complications are also not uncommon and gastric and intestinal ulceration may occur

Diagnosis.—This is best established by blood culture The causal organism has been isolated from the blood of a chronic case one year after the onset Agglutination tests are also of value provided they are properly controlled. Adequate control is especially important in hot [illegible]

at some time during the period of defervescence.

As already stated, the classical form of undulant fever is indistinguishable clinically from that due to the organism of contagious abortion For isolation of the bovine strain of *Br. abortus*, growth in an atmosphere of 10 per cent CO_2 is necessary, whereas the swine strain (*Br. suis*) will grow readily without this addition.

Differential Diagnosis.—Save where laboratory facilities are available, it is not always easy to diagnose undulant fever It is apt to be mistaken for typhoid, paratyphoid, sub-tertian malaria, influenza, hepatic abscess, tuberculosis, especially phthisis, and, in certain regions, kala-azar

The history and careful clinical observation will usually help to clear up the case, but in no disease is bacteriological investigation more important.

Prophylaxis.—As for typhoid, special attention being paid to the disinfection of the urine Isolation of human carriers, if they can be found Boiling goats' milk, use of tinned milk, the slaying of infected goats, and the avoidance of local products of milk

Personal cleanliness as a preventive is important.

Treatment—No drug has any specific action on the disease Yeast may be given in 2 drachm doses twice daily in the hope of increasing the polymorphs and reducing the tendency to neuritis Marmite in drachm doses [illegible] of benefit in the recent [illegible]

to be combated by the usual hypnotics, and cardiac tonics are often indicated Cold sponging and local anodynes for joint and nerve pains are useful Depressing drugs such as quinine and the salicylates are harmful The tervalent antimonial preparation, Fouadin, has given good results in some hands Striking results in some cases have been

claimed with drugs of the sulphonamide group; in others they have not been so successful.

500 c cm. of blood transferred from a convalescent patient has been favourably reported on. Protein shock therapy (intravenous T.A B, etc) has also given good results

YELLOW FEVER

West Africa appears to have been the original home of yellow fever, whence slave ships imported the disease to the Americas. Here the first identifiable epidemic broke out in Barbados in 1647. It established itself in endemic foci in the Southern United States, Mexico, Central America, along the coasts of tropical South America, and in the West Indies. From these localities widespread epidemics originated, involving southern Europe on many occasions, and at least one outbreak occurred in the British Isles, namely in Swansea in 1865, due to infection imported from Cuba by the ship *Hecla* Although the range of yellow fever is much [illegible] of Central and [illegible] pathologically'' It should [illegible] the Fourth Interim Report of the Inter- [illegible]

the 15° N parallel of latitude, thence eastward along that parallel to the eastern border of the Anglo-Egyptian Sudan, thence northward along the north-western boundary of Eritrea to the Red Sea coast, thence southward along the eastern coast of Africa to the southern boundary of the Protectorate of Kenya, thence westward along that boundary and the southern boundary of Kenya Colony to its junction with the southern border of the Uganda Protectorate, and thence along this and the eastern border of the Belgian Congo to the 10° S parallel of latitude, thence westward along that parallel to the west coast of [illegible] to the mouth [illegible] The [illegible] rthern [illegible] Eritrea [illegible] issawa

should be regarded as excluded from that area, and that restrictions under the International Sanitary Convention, 1926, should not be applied to ships proceeding from this port to other ports on the ground that such ships have come from a yellow fever infected port or one in close relation with an endemic centre of yellow fever. The Committee

make this recommendation subject to the proviso that *Aedes* control measures at the port of Massawa are maintained."

Etiology.—Yellow fever is due to a virus which is present in considerable concentration in the human blood stream during the latter part of the incubation period and during the first three days of fever. Usually the blood is not infective after the end of the third day since the virus is then neutralized by immune bodies Aragao, in his researches in Brazil, injected susceptible monkeys with the blood of sixteen patients after seventy-two hours' illness He obtained only four positive results

The virus when present in the blood is filterable through Berkefeld V and N filters, its size, accurately estimated by passing through graded collodion membranes is from 18 to 27 mμ

After an infective feed an *Aedes ægypti* mosquito is not capable of transmitting infection by bite for some days, the period varying in relation to the temperature It may be as short as eight, as long as fifteen or more days, the average being about twelve days The insect is then infective for the rest of its life, on an average about two months *Aedes ægypti* cannot transmit the virus to its offspring, while contact infection from one mosquito to another does not occur.

The only proven vector of the disease in Africa is *Aedes ægypti* (=*Stegomyia fasciata*), a house-haunting species spread widely, but in the New World intermittently, between the latitudes of 40° N. and 40° S (Fig 13) It is most active in the afternoon and in the early morning, but if hungry may bite at any hour. A number of other African species of mosquito have been found capable of transmitting yellow fever by bite under laboratory conditions, but their rôle in nature is at present unknown These experimental carriers are . *Aedes* (*Aedimorphus*) *stokesi*, *Aedes* (*Stegomyia*) *africanus*, *A* (*S*) *luteocephalus*, *A.* (*S*) *simpsoni*, *A* (*S*) *vittatus*, *Eretmopodites chrysogaster*, *Tæniorhynchus* (*Mansonioides*) *africanus*, and *Culex thalassius* Among mosquitoes universally distributed in the tropics and capable of acting as vectors under laboratory conditions is *Culex fatigans*, while *Aedes albopictus*, found in India and the Far East, can also transmit the virus by bite The means by which infection is maintained in endemic foci is still uncertain There is, however, considerable evidence to show that the virus may persist in the absence of human infections In the endemic zone in Africa and in South America about 20 per cent of wild monkeys are found to have immune bodies to yellow fever. African monkeys are not insusceptible to yellow fever but the disease in them is inapparent, although the virus may circulate in the peripheral blood stream for a few days There is some evidence that both wild and domestic animals may become infected under natural conditions: in fact it is now generally believed that yellow fever is primarily a disease of animals which only on occasions attacks man. The introduction of a sufficient number of susceptible persons, however, provides the necessary combustible material for an epidemic.

Jungle Yellow Fever.—It has been proved that yellow fever occurs in many forest districts in South America where *Aedes ægypti*, which is primarily an old-world species, has never penetrated Jungle yellow fever has been described more especially in Brazil and Colombia I

must be distinguished from rural yellow fever, the only known vector of which is, as in urban epidemics, *Aedes ægypti*. In South American jungle yellow fever, although the virus is identical with that causing urban outbreaks, the proven vectors are *A. leucocelænus*, *Hæmagogus* [illegible]

Symptoms.—The incubation period is usually from forty-eight hours to just over six days, but may extend to as long as ten days. Occasionally prodromal symptoms, malaise, headache, and giddiness, are in evidence for a day or two, but the onset is usually abrupt, sometimes with a feeling of chilliness which may amount to a rigor. There are marked frontal headache, perhaps so intense as to make the patient cry out, and racking pains in the back and limbs As the temperature rises, the face, at first pale, becomes red and turgid, and the eyes bright and watery, with fine injection of the conjunctivæ. The eyelids are swollen and drooping. The appearance of the patient may suggest scarlet fever, an error which in one instance was directly responsible for almost 150 deaths. During this time the temperature rises and reaches *its maximum*, usually after about twenty-four hours, or a little longer. Temperatures over 104° F are very rare in yellow fever. As a general rule those whose temperature does not rise above 103° F. recover. As a rule the pulse is rapid, but even at this early stage it may be slow in relation to the temperature The muscular pains increase in severity and the patient may feel as if he had received a knockout blow—the "*coup de barre*" of old writers The appetite is lost, the skin hot and dry, the tongue small, pointed, furred but with clean edges, and constipation is the rule. The patient is sleepless, restless and anxious. There is marked epigastric discomfort and tenderness, and vomiting of mucus, bile-stained fluid, or pure gastric juice commences ("white vomit"). The urine is diminished, and albumin, *in increasing amount*, appears usually on the second or third day.

The foregoing symptom-group constitutes the First Stage.

The Second Stage, that of remission, commences usually between the third and fifth days, and is characterized by a fall in the temperature and abatement of the symptoms. The redness and turgidity of the face disappear, and the conjunctivæ lose their suffusion but generally become icteroid. The attack may end here, but usually after a lull of from a few hours to a day or two, vomiting recommences, the temperature rises, and the patient enters on the Third Stage.

The outstanding features of the Third Stage are black vomit, melæna, and jaundice The vomit varies from a clear liquid containing dark flakes, to a thick uniform black fluid. Jaundice of any shade of yellow [illegible]

is prolonged, that is to say, most frequently in cases of recovery. The urine diminishes in quantity and the albuminuria continues to increase. There is often a marked dissociation of the temperature and the pulse rate. With a constant temperature there is a falling pulse rate, with a

rising temperature the pulse rate is constant. In addition to the black vomit, other hæmorrhagic signs are common—melæna, purpuric spots, bleeding of the gums, lips, tongue, bladder, vagina—and vision may be destroyed by extravasation of blood into the eye. Toxæmia increases, hiccup sets in, and the patient dies in a state of exhaustion, coma, or convulsions.

In more favourable cases, improvement may set in during the third stage, the unfavourable symptoms ameliorate, and convalescence is rapidly established. According to the degree of severity of yellow fever, three clinical grades have been described:—

Mild.—Even in Europeans the attack may be so mild as to be mistaken for influenza. Slight headache and backache with fever lasting for forty-eight hours may constitute the only symptoms. Albuminuria may be entirely absent or very transitory.

Severe.—The appearance in the stage of remission of the characteristic symptoms—jaundice, vomiting, hæmorrhages, anuria, mental disturbance, slow pulse.

Grave.—The symptoms just detailed appear during the first stage. There is marked involvement of the nervous system. The attack may assume a "pernicious" type, with apoplectic, choleraic, or algid symptoms. In the last-named there may be no jaundice.

Morbid anatomy.—The only specific changes are found in the liver. In patients dying in the acute stage the following microscopical changes are found. A jumbling of the trabeculæ, as if the liver cells had been thoroughly shaken, more accentuated in the mid-zone of the lobule than elsewhere, fatty degeneration of varying intensity generally more abundant in the central and peripheral than in the mid-zone of the lobule, an absence of complete necrosis of the central zone of the liver lobule, a few non-necrotic cells can always be found among the cells immediately adjacent to the central veins even when at first sight all the cells seem to have undergone an acidophilic change, what has been called a "salt and pepper" distribution throughout the entire lobule with greatest prevalence in the mid-zone of rounded refractile acidophilic bodies, the so-called Councilman bodies. These acidophilic bodies sometimes show the "shadows" of nuclei within them, they are the remains of parenchymatous cells that have undergone a specific type of necrosis. Other changes in acute cases are a varying degree of leucocytic infiltration, principally of mononuclear cells, most pronounced in the mid-zone, yellow pigment inside the parenchymatous cells of the central zone, hyperæmia of the sinusoids, especially in the mid-zone, nuclear changes. The nuclear changes consist of œdema and intranuclear inclusions; the latter consist of acidophilic material and are associated with margination of the basophilic chromatin on the nuclear membrane. Intranuclear inclusions are not well preserved by material fixed in formol or formol saline, and Zenker's fluid, without acetic acid should be used whenever possible, portions of liver to be fixed should not exceed 1 c.cm. Intranuclear inclusions are only seen in about 20 to per cent. of human liver cells, except in some epidemics, as in Accra 1937, when 70 to 80 per cent. of the liver cells exhibited this change.

In patients who have died after the eighth day of illness there may be only a few Councilman bodies, but their place is taken by masses of bright ochre-coloured granules lying either free among the non-necrotic parenchymatous cells or more often within macrophages and Kupffer cells. These ochre-coloured bodies are the last stages of degeneration of the hyaline Councilman bodies, probably impregnated with bile pigments

Diagnosis.—It should be emphasized that there is no one clinical feature which is characteristic of yellow fever. Exact diagnosis of yellow fever can only be made by one of the three following methods:

(1) Isolation of the virus from the blood during the first three days of fever.

(2) Histological examination of the liver in fatal cases.

(3) A mouse-protection test for immunity, blood being taken during the first few days of illness and again during convalescence

(1) Isolation of the virus can only be carried out as long as the virus is present, free in the blood, unneutralized by antibodies.

The following animals are susceptible: the Indian rhesus monkey, *Macaca mulatta*, hedgehogs, both the European and various African hedgehogs, and the mouse.

Monkeys and hedgehogs should be injected with 1 c cm. of blood intraperitoneally, monkeys should have their temperatures taken daily, a temperature of 104° F. or over is significant The disease in monkeys usually takes about three days to develop and death may occur from three to four days later. Hedgehogs die in from seven to twelve days; both in rhesus monkeys and hedgehogs the lesions are similar to those found in man. Some strains of the yellow fever virus, however, cause neither fever nor death in rhesus monkeys, if these animals are inoculated blood should therefore be removed from the heart on the fifth day after inoculation and serum injected into mice. When mice are inoculated with yellow fever blood, they should be injected intracerebrally with 0 03 c cm of serum, the point of inoculation being over the vertex of the skull and just to one side of the middle line. If newly-born mice are available they can be inoculated intraperitoneally. Symptoms of encephalitis begin to develop in from nine to twelve days; death taking place two or three days later.

In removing blood from patients with suspected yellow fever, it is important that rubber gloves should be worn unless the operator has himself been immunized. If the blood is to be forwarded to a laboratory it should be placed in a thermos flask and packed with ice and salt.

(2) Portions of liver can be removed without carrying out a full post mortem by means of an instrument known as a viscerotome. Viscerotomes are now widely used in South America and are available in Africa. Many Africans, both Mohammedans and pagans, object very strongly to mutilation of the corpse after death

Extensive burns may give rise to liver changes not unlike those seen in yellow fever

(3) The mouse-protection test. This test, which is highly specific for immune bodies to yellow fever, consists in the injection of mice with a

neurotropic strain of the yellow fever virus and the serum to be tested. If the serum contains immune bodies the mice survive. By using dilutions of serum the test can be rendered quantitative. A single positive mouse-protection test signifies that the patient has at some time or another become immunized against yellow fever. A negative test at the beginning of an illness and a positive test during convalescence show that the illness must have been due to yellow fever. At least 1·5 c cm of blood should be removed for a mouse-protection test. The blood should be allowed to clot and no preservative should be added. The test is extensively used in yellow-fever surveys. To determine whether yellow fever has recently been active, the sera of young children are examined. The test is also used if it is necessary to confirm that a given batch of yellow fever vaccine has actually conferred protection on those inoculated.

Differential Diagnosis.—Leptospiral jaundice: Leptospiræ can be isolated from the blood and urine, and the infection is easily transmitted by inoculating the scarified skin of the guinea-pig. In leptospiral jaundice there is almost always a polymorphonuclear leucocytosis, in yellow fever almost always a polymorphonuclear leucopenia. Malaria, blackwater fever, relapsing fever and any short fever with jaundice, have to be distinguished. Infective hepatitis is common throughout Africa, occasional patients may develop jaundice and black vomit, dying with acute or sub-acute liver necrosis. Dengue, also transmitted by *Aedes ægypti* and therefore to be met with in the same districts as yellow fever, bears a strong resemblance to a mild attack of the latter disease. In the Greek epidemic of dengue some severe cases had jaundice and black vomit. Durand's disease, a virus infection described in Tunis, may also cause black vomit, while Rift Valley fever, Bwamba forest virus, and West Nile virus may simulate a mild attack. It should be remembered that many Africans develop jaundice with lobar pneumonia, while sickle-celled anæmia may also cause acute attacks of jaundice.

Treatment.—Every drug likely to be helpful has been tried in yellow fever, but none yet discovered has any curative effect. Rest the stomach as far as possible, avoiding milk, and give iced water, iced sugar water, or alkaline drinks, in the hope of preventing mechanical blocking of the kidneys. An ice-bag applied to the epigastrium is sometimes of marked benefit in relieving distress. Intravenous injections of 5 per cent. glucose, half a pint at a time, have much to commend them if glucose cannot be taken by the mouth. When large quantities of glucose are being taken five to ten units of insulin daily are of value. The serum of convalescents or hyperimmune serum, if given during the incubation period may abort or at any rate reduce the severity of the attack. Such sera are, however, quite valueless in treatment once symptoms have been observed.

Prophylaxis.—There are three essentials in the prophylaxis of yellow fever:—

(1) Early diagnosis of cases.

(2) Immunization.

(3) Eradication of mosquitoes.

Early Diagnosis.—The methods necessary for *exact diagnosis* hav

already been described. If the first case or cases escape undiagnosed a second crop will appear in about a fortnight's time and an epidemic may rapidly assume gigantic proportions. In the Sudan outbreak of 1941 there were probably 50,000 to 60,000 cases. Despite its proportions, this epidemic was discovered by mere chance after it had been in progress for some months.

Immunization.—Immunization is carried out by means of a single inoculation of yellow fever virus vaccine. The vaccine is prepared by cultivating an attenuated strain of the yellow fever virus on the chorio-allantois of the developing chick embryo. The tissue-culture virus is dried by the low-temperature-reduced-pressure method and maintained in sealed ampoules. The virus is, however, still living and is relatively unstable. The vaccine will only retain its full potency if it is stored continuously at a temperature that is not raised above 0° C. During transportation special precautions are needed to ensure that a low temperature storage is maintained.

Unless the vaccine is active, immunity will not develop in the inoculated individual. When, therefore, it is necessary to store the vaccine for any prolonged period animal inoculation tests should be undertaken from time to time to ensure potency before use.

For administration, the vaccine is reconstituted by the addition of cold sterile normal saline. It is important to see that the sterilized syringe and needle are cool before the vaccine is taken up and also that any of the vaccine not used within an hour of reconstitution is discarded. Spirit or antiseptic of any kind must be kept from contaminating the syringes or needles.

Very large numbers of individuals have now been immunized in South America and West Africa, and also in this country and the United States before they proceed to West Africa. As a rule there is little or no reaction, only a very small proportion develop a slight headache and malaise some five days after the injection. Immunity develops about ten days after the inoculation and lasts for at least four years. The Inter-Departmental Committee on Yellow Fever Control, set up by the Secretary of State for the Colonies, has not only recommended large-scale immunization within the endemic zones in Africa, but has also recommended that all travellers passing through an actual endemic zone to a potentially endemic area should also be immunized. The endemic zone in Africa has been defined on p. 332.

Some batches of yellow-fever vaccine have been followed by a relatively high incidence of homologous serum jaundice (p. 140). Human serum was eliminated from the vaccine in 1943, since when further cases of post-vaccinal jaundice have not been reported.

Mosquito Destruction.—Known or suspected cases of yellow fever should be isolated in screened quarters or kept under mosquito nets night and day. All mosquitoes in infected houses must be hunted down and destroyed by every available means. All houses within a radius of at least 40 yards, and preferably more, of an infected house should be dealt with in this way. Everyone in the neighbourhood should use mosquito nets with great care unless their habitations are effectively screened.

Aedes ægypti is essentially domestic in its habits and breeds in and around houses in tanks, sagging gutters, tins, domestic utensils, flower vases, "crown corks", and every kind of vessel or container which holds water. This mosquito also breeds in tree holes, for example in baobab trees, *Adsanonia digitata*, at considerable distances from houses. If holes are numerous the trees should be felled, if there are only a few holes they should first be creosoted and the interiors then filled with earth and coalas or other liquid tar preparation. This does not crack in the way that cement does.

An intensive and tireless campaign must be waged against the vector in all its stages, fortunately it is the easiest of all mosquitoes to eliminate. It should be remembered that eggs withstand drying for prolonged periods and may hatch out months after being laid if they come in contact with water. (*See* Arthropod Pests and Appendix 1.)

Quarantine.—There is a danger of transporting either infected *Aedes ægypti* or persons incubating the disease from yellow-fever areas by air over long distances to countries so far free from the disease, and this has been reflected in the stringent regulations published and enforced by such countries as India and Egypt for dealing with the control of aircraft- and other passengers from yellow-fever countries.

Spraying of all aircraft from yellow-fever areas with an effective insecticidal spray is only one of the many important measures designed to prevent the spread of yellow fever from endemic areas to those in which yellow fever does not exist, but where there may be conditions which permit its development.

Aerodromes and nearby villages are strictly controlled and supervised to keep down mosquito breeding and to keep potential ambulant carriers of yellow fever well beyond the boundaries of airfields. (In the African, the disease can occasionally be so mild as to escape recognition.) During the 1939–45 war these measures were often hard to enforce, but large-scale immunization of passengers, aerodrome staff, and natives in adjacent villages conferred a much greater measure of real security than unenforceable measures of screening and quarantine. During this war, the Inter-Departmental Committee, whose fourth interim report has already been referred to, did valuable work in encouraging research and study of the yellow-fever problem and in proposing and securing wide agreement for the measures of control it put forward on expert advice. For full details the Fourth Interim Report (H.M.S.O. London, 1944) should be consulted. With the end of the war, the work of the committee may be expected to pass to some international organization.

APPENDIX I

USES OF D.D.T.

Because of its prolonged residual action D.D.T. has a wide range of usefulness against insect pests. But special techniques of application and a careful study of each insect problem are essential for success. This Appendix should therefore be read along with the accounts of the various insects (*see* Arthropod Pests).

ADULT MOSQUITOES

In general, anophelines are more susceptible to D.D.T. than culicines. A careful study of the local species and their habits will always assist in the choice of the best method of using D.D.T. for any particular situation.

Direct spray in buildings.—D.D.T. is used in direct sprays to augment the killing power of pyrethrum, which, by itself, ensures a quick knock-down of insects but is an uncertain killer. D.D T. alone gives a poor knock-down, the combination of both is highly effective. The addition of D D.T is particularly desirable in sprays to be used against flies as

[illegible]

controllable valve for the release of as much spray as may be required The dosage to be applied is expressed as emission-time of the spray, and is 4 seconds for each 1,000 cubic feet. Individual insecticide sprayers are

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seconds, and one sprayer is sufficient for 1,000 cubic feet.

The new aerosols include D D T. so that the spray is effective against flies as well as mosquitoes.

Much work is being done on the development of individual pocket-size sprayers (not aerosols) and the best results so far have been obtained with the following formula: 30 per cent. D.D.T.; 20 per cent. cyclohexanone, 5 per cent. motor oil, and 0 2 per cent. pyrethrins in kerosene. A comparison of aerosols with finely atomized sprays for use in large buildings indicated that spray atomized with a paint-sprayer nozzle was the better, particularly if the fine spray was discharged over a 16-inch fan.

Direct spray outdoors.—The wide use of aircraft-spraying of D.D.T has established the value of outdoor spraying in the destruction of adult mosquitoes that rest in foliage or other vegetation The results have been so dramatic that, in view of the residual action of D D T. on foliage, more and more importance is being attached to adult control as opposed to anti-larval measures

In salt marshes in the U.S A a 5 per cent spray applied by aircraft in a dose of 2 to 3 quarts of solution an acre has given 99 per cent. reduction of *Aedes* species Similar good results have been obtained against anopheline mosquitoes in India, Burma, and U S A. In Italy, however, where *An maculipennis* rests in stables, houses, and other buildings during the day, equally good results have not been obtained and this stresses the importance of studying the habits of the mosquito in relation to control measures The residual action from D D T deposited on foliage during aircraft spraying is very variable and not yet fully determined. Residual action on foliage following ground application is considerable (*see* Residual sprays outdoors)

There is some evidence that inclusion of a mosquito irritant like cyclohexanone in the aircraft spray stimulates the mosquitoes into flight with a higher kill in consequence Details of solutions used in aircraft spraying are given below (*see* Mosquito Larvæ—aeroplane applications)

Ground application of sprays has proved very effective either with aerosols or fine sprays atomized by paint-guns Using specially large aerosol containers workers in the U S A. have shown that aerosol spray can drift 800 to 1,000 feet over open country, and that with containers holding 300 to 400 pounds of solution 500–1,000 acres could possibly be treated Finely atomized sprays of 5 or 10 per cent solutions, discharged with hand-operated paint-sprayers, have given 95 per cent. control of adult mosquitoes with quantities as small as 240 c cm an acre. But to ensure proper coverage of the treated area, sprays used in this way should normally be applied at not less than one pint an acre

Residual sprays indoors.—The prolonged residual action of D.D T is of the greatest value for adult mosquito destruction Solution- or emulsion-sprays applied direct to the walls of barns, stables, houses, tents, native huts, and other buildings have proved very effective. Field experience in Italy, India, Assam, New Guinea, and West Africa, seems to agree that 50–100 mg of D D T a square foot (1–2 c cm of 5 per cent solution) is very effective up to two months after application

The reduction of adults after residual spraying often leads to considerable reduction of larvæ as well In Arkansas a residual deposit of 56 mg of D D T. a square foot reduced the adult density of *An quadrimaculatus* by 99 per cent for 1½–2 months and the larval density by 66 per cent

The effect of the type of wall surface under treatment has not been fully determined Good results have been obtained on plaster, brick, wood, and corrugated-iron surfaces, and on tents One report states that residual sprays on thatched native huts have a shorter persistent action than on mud-walled, metal-roofed houses

The need for studying the habits of the local mosquitoes is emphasised by experience in New Guinea with *An punctulatus* Females of this

species do not normally rest in houses; but if they enter a house in search of a blood meal, they often rest for a short time before or after feeding, and so offer a chance for their destruction by D D.T. sprayed on mosquito nets, furniture, and the like.

Residual sprays outdoors—This section is closely linked with that on direct spray outdoors (*see* above). Residual effect after aircraft spraying is very variable, being dependent on density of foliage, rainfall, and other factors In India, residual effects from 5 to 12 days have been recorded after spraying 2 to 3 quarts of 5 per cent. solution an acre.

Aerosols released at 1–2 feet from the ground can be used to put a mosquito barrier around temporary camps and in some cases this has given 95 per cent. reduction in mosquito density. In one case a barrier of 100 feet wide around a half-acre site was sprayed with 10 gallons of 5 per cent. solution (barrier of 2 4 acres). Twenty-eight days later there was an 87–99 per cent. reduction in adults of *Ae. taeniorhynchus* within the barrier zone, and 30–80 per cent fewer mosquitoes within the inner untreated zone The result is of particular interest because *Ae. taeniorhynchus* is a much stronger flier than most anophelines

The ground sprays can be used within semi-permanent camps, a dose of 5 gallons of 5 per cent. solution an acre being effective for one month in maintaining an 80 per cent. reduction in mosquito density.

Emulsions.—Preliminary experience has shown that emulsion-sprays are as effective as solution sprays and can be used in the same dosage and technique of application for the same purpose Emulsions are of value because they conserve supplies (the oil solvent is largely replaced by water) and save the shipping space and transport needed for bulky material. With our increasing experience emulsions will more and more replace solutions, particularly in distant parts of the world.

MOSQUITO LARVÆ

In general the application of 2 to 4 ounces of any form of D D T. to one acre is enough for the control of both anopheline and culicine larvæ. Higher concentrations may be required for residual action, but the evidence is still conflicting about how long it is possible to make the action persist. Weather conditions so affect dispersal of D D.T. that many consider it inadvisable to rely upon any residual action against larvæ except in special circumstances At present, it is considered that heavy doses (0 5–1 0 pound of D.D T. an acre) are wasteful and that their use is unwarranted except in forward areas to protect fighting troops. Even in these conditions better results can usually be secured by anti-adult measures.

Solutions.—In the China-India-Burma theatre ground application of [illegible] quart an [illegible] It In [illegible] water

though twice the recommended dose had to be used, the action did not persist beyond two weeks. Good results have also been obtained in Assam (in slow moving streams), Panama, and Florida. In Australia effective control was obtained with 1 0–1 25 pints of 4 per cent D D.T. an acre if the whole dosage was actually applied to the water surface.

All accounts stress the importance of ensuring adequate covering of the water. Difficulties in applying small quantities of liquid with existing equipment have led to the use of 2 per cent. D.D T solutions at a rate of 5 quarts an acre, rather than 5 per cent solutions at 2 to 3 quarts an acre Kerosene or Diesel oil No 2 are the commonest and most usually available solvents, waste oil is also useful (*see* below Preparation of D D T solutions in the field)

Applications by drip cans, squirt cans, oiled sawdust, sacking, and single-point methods are less efficient variants of the usual spray technique. Their effect depends on the spreading power of the diluent oil and the density of vegetation It is essential to check results by dipping for larvæ.

Emulsions.—These are used in exactly the same manner as solutions, and at the same rate of application Besides their other advantages (*see* above) the water for dilution of emulsion concentrates is easily obtained and the rate of dilution can therefore be readily varied to suit local conditions, a minimum of 2 to 4 ounces of D D T. an acre must always be applied. In America it has been shown that emulsions are more effective than solutions against culicine larvæ

Dusts.—For dusting, there is no advantage in using D D T. in place of Paris green, except the difference in dosage (2 to 3 ounces of D D T against 0 5–1 0 pound of Parish green an acre) There is some evidence that D D T. dusts are effective against culicine larvæ because some of the D D T. sinks, but this advantage is largely offset by the tendency of D D.T. dusts to form lumps, they are not spread from aircraft for this reason

Aeroplane Applications—For aircraft applications, solutions are used almost exclusively although emulsions may soon be available As explained, dusts have not been used because they tend to form lumps or "balls".

[illegible]

Dosages five times greater than the normal gave a residual action for only two weeks It is agreed that duration of residual action depends on [illegible]

It can be accepted that the normal dosage rate is 2 to 3 quarts of 5 per cent D.D.T. solution an acre. Solutions in kerosene or Diesel oil No. 2 have been used successfully; useful addition are: oleic acid (0 5 per cent), castor oil (1 0 per cent), or similar agents to aid spreading ... aircraft solutions are being used, but no special standard solut[illegible] available. American workers have found the following suitable f[illegible] situations. 5 per cent. D D T.; 5 per cent cyclohexanone; 45 pe[illegible] lubricating oil, and 45 per cent. No. 2 fuel oil.

SANDFLIES

From experiments in the Middle East it would appear that alm[illegible] complete protection against sandflies can be obtained by D.D.T. resid[illegible] spray. The dose recommended is 50–100 mg a square foot of surfa[illegible] (1 to 2 quarts of 5 per cent. solution to 1,000 square feet) The inside wal[illegible] should be sprayed from floor to ceiling and as much of the ceiling as possible should also be sprayed. Special attention is given to corners and upper parts of the walls, doors, windows, and screens.

In the classical situation, where sandfly shelters and breeding-places are closely associated with human habitations, outside spraying of walls and rubble heaps alone gives a high degree of local control by denying the principal outdoor shelters and breeding-places and destroying the sand flies before they can enter buildings.

The larvæ, which are protected by soil and debris, and breeding-places at a distance are not affected, but by combination of indoor and outdoor spraying adults are destroyed in great numbers. The long life-cycle of the sandfly, the low replacement-rate, and the constant adult-destruction by the D D T -treated surfaces all favour the achievement of area control.

FLIES

D.D.T. is of particular value for controlling flies of many different species. It acts only on the adult fly; eggs, larvæ, and pupæ are unaffected

Against flies, D.D T. can be used in a variety of ways but there are three common methods: as a direct spray, as a residual spray, and in any form on breeding-areas where flies gather to lay aggs.

The amount of D D.T. required is the most important factor to be determined. In the treatment of breeding-areas especially, the amount of D D T. in the dust or liquid can be varied a good deal to suit local conditions. The object of D D.T. treatments is to reduce the density of flies, not merely to kill individual flies. The full effect of a residual spray or dust in reducing the density may not be achieved for 5 to 14 days after application, much depends on temperature and weather conditions. For many weeks after it has ceased to affect the general density, residues of D.D T will continue to kill some flies

Direct Spray.—Anti-mosquito spray containing pyrethrum only is of little value against flies, but the addition of 0 3 per cent. D D.T. gives a very effective spray. The pyrethrum gives the quick "knock-down" and the D D.T. kills the flies. Plain D D T. sprays have no knock-down; therefore, an effect is not seen until about 15 minutes after spraying, and

some flies are not affected until 45 minutes. Solutions and emulsions are equally effective, if pyrethrum is not available they should be used at 0 5–1 per cent. strength. Repeated application of direct sprays leads to a building-up of D.D T on exposed surfaces so that a residual effect is eventually produced

Dust.—D D T. dust is most effective against flies when applied to breeding-areas; in buildings it is most useful as an insecticide against cockroaches. If we estimate weight for weight of D D.T, solutions and emulsions are more effective than dusts, but a good residual action can be obtained by using 1 to 2 grammes of D D T in dust form for each square foot.

Residual Spray.—For fly control D D T. is best used as a residual spray This can be applied to any surface on which flies tend to alight, such as cookhouses, food-stores, stable walls and doors, living-rooms, manure-heaps, refuse-pits, and so forth The effect on manure-heaps and similar places is governed by the frequency with which manure is added to or taken from the pile, for the D D T surface can act only if it is not covered or removed. Experiments on walls have shown that with 50 mg of D D T. a square foot flies are killed for at least six weeks, and sometimes for as long as 17 weeks. In fly-proofed cookhouses and indoor mess-halls it has been found that after applying D D T. at this dosage it is unnecessary to use insecticidal sprays for at least one month The dosage advised for actual use is higher than this 100 mg a square foot

Solutions or emulsions can be used as residual sprays in concentrations of 1, 2, or 5 per cent, depending upon the amount of D D T required on the surface and the apparatus available for spraying Any readily volatile solvent that does not have a persistent odour can be used, kerosene is generally chosen

BEDBUGS

Bedbugs have been eradicated from various types of building with D D T residual sprays Although direct spraying will kill some bugs this cannot ensure penetration of the numerous cracks and crevices where the insects rest and breed, residual sprays, therefore, should always be used Dusts are useful but less effective than solution- or emulsion-sprays

The spray should be applied very thoroughly to all mattresses, bedding, beds, and cracks and crevices in the walls, in a dosage of 200 mg of D D T a square foot This concentration has proved effective in preventing reinfestation for six to nine months Eggs are not affected but the young bugs will be killed as they hatch out and come in contact with the insecticidal film on walls and beds The lethal action requires some time so that the kill of bugs may not be complete until 48 hours after spraying

COCKROACHES

There is some difficulty in cockroach control because these insects are highly mobile and premises are easily reinfested Residual sprays of

D D.T. are a valuable new method of control, but dusts are of more valu against cockroaches than against most other insects because of the habits of cockroaches.

The spray (5 per cent.) or dust (10 per cent) should be applied liberally, in a dose never less than 100 mg. of D D.T. a square foot. The German cockroach (*Blatella germanica*), which is light brown and smaller than the other species (about half-an-inch long), is more resistant to D D.T. than the *other* common roaches. Duration of residual action of D D.T. is not fully known but it is much shorter against roaches than for any other insects.

LICE

The outstanding success of D.D.T. up to the present time has been i use in louse control, notably during the typhus epidemic at Naples i 1943–44. In Naples, insecticides such as AL63, MYL, and later, D.D.T. anti-louse powder were applied by hand and dust-guns to over 2,750,000 civilians Undoubtedly these powders were important contributions to success in controlling the epidemic. Lice and louse-borne typhus need no longer be a serious menace to any army in the field.

The arrival of D D T. has changed delousing policy in the British Army, steam-disinfestation being now reserved for the clothing of typhus patients and close contacts. In all other circumstances anti-louse powder is us-

Anti-louse powder.—AL63 Mk III was 5 per cent. D D.T. in kaol (china clay) but the anti-louse powder now in use contains 10 per cen D.D.T. It can be used for control of body lice by individual soldiers, who *rub* the powder into the seams of underclothing and sprinkle it lightly over the surface, especially of garments worn next to the skin, or it can be applied by hand- or power-operated dust-guns to *fully* clothed persons (for details *see* Arthropod Pests—Lice).

The great advantage of this method over steam or hot air is its speed, because the individual can be deloused while fully clothed; it is *only* necessary to loosen the jacket, shirt-collar, and trousers.

One treatment will quickly and effectively reduce the lousiness of a community, but it must be remembered that three treatments are needed at weekly intervals for complete elimination of all nits and lice. When complete disinfestation is required, all clothing and blankets of each individual should be dusted at the first treatment; at the two *subsequent* dustings the individual may be treated without being undressed. One treatment with anti-louse powder *will* prevent reinfestation Care should be taken to see that men who have been treated do not immediately discard, change, or wash the dusted garments.

When large numbers need treatment—prisoners of war, refugees, or civilians employed by the Army, *for* example, the treatment should be carried out by specially trained dusting-teams. Each unit consists of one N C O. and five other ranks equipped with six hand dust-guns or a mechanical air-compressor operating two dust-guns; these units are normally attached to a Field Hygiene Section or Sanitary Section. Dust-guns in addition to those held by anti-typhus units are on issue to all R.A.M.C. units.

It is essential to follow a proper routine in order to distribute the powder on the inner surface of the inner garments, especially of those covering parts most frequented by lice, such as armpits, shoulders, waist and crutch The side seams of shirts should always have attention

The D D T powder can also be used for head lice by applying it directly to the head and nape of the neck, and for pubic lice by applying it to the pubic and perianal regions and to other hairy parts of the body like the armpits

Impregnated clothing—In the British Army angola drab shirts are impregnated with D D T at the rate of 1 per cent of D D T, weight for weight of the garment The shirts, referred to as shirts A/T (anti-typhus), have been shown both experimentally and in the field to be the most powerful anti-louse measure at present known They are almost indistinguishable from non-impregnated shirts, free from unpleasant odour, and without any harmful effect on the human body The shirt A/T derives its value from three considerations —

1. If unwashed it will afford complete protection against lousiness for eight weeks and considerable protection for a further four weeks.
2 Any combination of underwear can be worn underneath the impregnated shirt without affecting its insecticidal efficiency
3. The period of effectiveness is determined by the washing of the shirt Washing by the process of a Mobile Laundry Unit (MLU) destroys the insecticidal efficiency of the shirt after its third washing, but there is no material loss of efficiency up to and after the second wash Hand-washing removes the insecticide after four washes, the shirt remaining effective up to and after the third wash

The original impregnation of shirts A/T is carried out in the United Kingdom Re-impregnation in the field can be done by MLUs during the normal washing process with emulsion ATSO-I or II (Anti-typhus-soluble-oil), this does not involve the need for any special equipment MLUs attached to formations issued with shirts A/T should normally re-impregnate all shirts as a routine procedure

When the supply of shirts A/T is insufficient to cover an entire force, priority of issue should be given to troops most liable to become infested because their hygiene facilities are restricted by the conditions of service. The normal order of priority is fighting elements of divisions, all divisional troops, and units in close contact with civilian labour, e g Docks Operating Companies, units of the Pioneer Corps, and General Transport Companies, RASC

When shirts A/T are in use careful attention should be given to administrative arrangements, otherwise the troops will be denied maximum benefit from these garments Points that need special attention are —

1. The scale of issue should be two shirts A/T for each man, all other shirts should be withdrawn.
2. Issue should be made to whole units or formations, never to parts of units or to individuals.
3 Reinforcements to units should be issued with shirts A/T under unit arrangements, and non-impregnated shirts withdrawn

4 When laundering is done by MLUs or the troops use clo exchange points, arrangements should be made beforehand to en that units or individuals receive new or re-impregnated shirts A/ exchange for dirty shirts.

5 The ATSO-I or II emulsions, which are specially designed for impregnating shirts in the field, are issued if available to all MLU so that all shirts washed by the MLUs are automatically re impregnated

Liquid Preparations.—A number of liquid preparations containing D D.T have been recommended for the treatment of lice. They can be used in special circumstances; but the other methods of treatment are better and generally easier to use.

The liquid preparations, if liberally applied direct to the skin or hair, will destroy lice and eggs within six hours of treatment. To ensure a complete kill the patient should be told not to wash the treated areas for at least 24 hours. For head lice the dosage required will vary with the amount of hair, 10–15 c cm. for each treatment being usually adequate For elimination of pubic lice all hairy parts of the body should be included in the treatment; the perianal hair is often forgotten.

FLEAS

As a liquid or dust D.D T. is effective against adult and larval fleas. For control of larvæ a 5 per cent. spray applied at a rate of not less than 100 mg D D T a square foot is adequate. The spray should be applied to the floor and 3 feet up the walls Adult fleas can be killed by treatment of the individual and by spraying or dusting beds, bedding, and floors. In the typhus epidemic at Naples, it was clear that the widespread use of D D T anti-louse powder reduced the incidence of fleas to negligible proportions

MITES, CHIGGERS, AND TICKS

D D T is not of value for the control of mites or chiggers. It is effective against some species of ticks, but its value as a practical measure of control remains to be decided

PREPARATION OF D.D.T. SOLUTIONS IN THE FIELD

Crude D D.T. should always be kept as cool as possible. The crushing, sieving, and weighing processes described below should be carried out in the shade or under cover so that the powder does not become soft or sticky. With recent developments in D D.T., this risk is now less than it was

1 The crude D.D.T should be broken up by placing the powder on a tiled or smooth concrete floor, or on flattened sheet metal, and crushing the lumps by rolling a nail-studded board over it—the nails protruding not more than three-quarters-of-an-inch from the board. In this manner, the lumps of D D T. are broken up without grinding or pressure, which is liable to produce soft, sticky masses that dissolve only with difficulty.

2. After being crushed, the D.D T powder should be sieved or separated in order that any lumps exceeding one-eighth-of-an-inch may be rejected and recrushed.

3 The finely divided D D T powder should be weighed and then creamed to form a smooth paste by adding small quantities of kerosene or Diesel oil The powder should never be added direct to the bulk of oil After creaming, the D.D.T.-kerosene paste can be added direct to the bulk.

4. To assist in dissolving the D D T and to prevent layering, the container should be turned immediately on addition of the D.D T cream and at frequent intervals subsequently The containers should be exposed to the sun in order to raise the temperature of the oil and thereby assist in dissolving the powder It is important to allow a period of not less than 96 hours for solution of the D D T

5. To prepare the usual 5 per cent D D T solution, use half-a-pound of finely divided D D T to 1 gallon of kerosene or Diesel oil

IMPROVISED METHOD

1. With low heat melt the correct weight of D D T in a clean tin or bucket over a small flame or hot plate, and then pour the molten D D T into the cold paraffin, stirring all the time Solution is immediate For example, five pounds of D.D T should be slowly melted and poured while molten into an open tin containing 10 gallons of kerosene.

2. Care should be taken to see that the D D T is melted over a small flame, because, like many organic chemicals, D D T is volatile at very high temperatures

3. Absolute cleanliness of the receptacle is essential because rust has a catalytic action and will cause rapid decomposition of D D.T

4 Any smell of hydrochloric acid is evidence that decomposition of D D.T is already in progress.

APPENDIX II

ZOOLOGICAL NOMENCLATURE

It is hoped that the following notes will be helpful to medical officers in writing reports which necessitate the employment of names of animal parasites

The present system of binominal nomenclature was formally introduced for the animal kingdom in 1758 by the great Swedish naturalist Linné, usually known in this country under the latinized name, Linnæus On the Linnæan system the present International Rules of Zoological Nomenclature are based.

These were adopted by an International Congress of Zoology, and later congresses appointed a permanent International Commission on Zoological Nomenclature which concerns itself with the various questions arising in connexion with the Code.

Before dealing with any of the actual rules, it might be well to give a simple explanation of the method of classification adopted for animals. Take as an example the common fly, *Musca domestica*. All individuals included within this conception resemble one another in every specific point, other than such differences as are due to sex and to slight individual variation. Under suitable conditions these flies will breed and produce fertile offspring. *Consequently they are regarded as constituting a species, M domestica* Out of doors in England we are often pestered by flies resembling *M domestica* very closely, but whereas the male *M. domestica* has a fairly broad space between the eyes, this other fly has his eyes set

same arrangement of certain bristles, etc, characteristics which are sufficiently distinct to be considered of generic importance. So all the species showing these are grouped together to form a genus, *Musca*.

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found to have certain features in common, and so all which show these ... are grouped together in a family—MUSCIDÆ. By a similar

the

by a

similar grouping being the parasitic flat worms, parasitic round worms, molluscs, etc. And this pedigree carried back still further will ultimately join up with that of the more lowly animals, the PROTOZOA, this final assemblage of METAZOA and PROTOZOA constituting the animal kingdom.

For convenience in classification, divisions intermediate between these

may sometimes be recognized—suborders, subfamilies, subgenera, etc., and the individuals of a species, especially one which is large and widespread, may show small constant differences indicative of racial varieties or subspecies.

The individual specimen on which the original description of a species is based is known as the "type" of that species. The modern founder of a species deposits the type in some museum or collection where it is available for future reference. Unfortunately the types of many of the older species are now non-existent or unknown, a deprivation which may render the original verbal description difficult to interpret Similarly a definite species is taken as the type of a genus, usually, though not necessarily so, the earliest named species in the genus *Culex pipiens*, for example, is the genotype of *Culex*, and although this genus subsequently may be expanded or contracted, the generic characters of *Culex*, however regarded, must be such as to include the genotype, *C pipiens*

We may now consider the rules of nomenclature so far as they concern us

Article 2.—"*The scientific designation of animals is uninominal for subgenera and all higher groups, binominal for species, and trinominal for subspecies*"

Thus, human head and body lice belong to the genus *Pediculus*, the species is *Pediculus humanus*, and if desired to go further and contrast the two subspecies a trinominal designation is necessary, *e g. Pediculus humanus corporis* (Article 17 directs that when a subspecific name is cited it is to be written directly after the specific name without the interposition of any mark of punctuation)

Article 3 "The scientific names [illegible]

[illegible]

genus of ticks is correctly rendered *Ornithodorus* There is no objection to the terminal Greek *a*, therefore it is unnecessary to Latinize the common *-stoma* to *-stomum*

Article 4.—"The name of a family is formed by adding the ending *idæ*, the name of a subfamily by adding *inæ*, to the stem of the name of the type genus."

Thus from *Culex*, the type genus of the mosquito family, we have CULICIDÆ and CULICINÆ.

Article 8.—"A generic name must consist of a single word, simple or compound, written with an initial capital letter, and employed as a substantive in the nominative singular"

Article 10.—"When it is desired to cite the name of a subgenus, this name is to be placed in parenthesis between the generic and specific names"

Many authorities regard *Stegomyia* as a subgenus of *Aedes*, which would be expressed by the form, *Aedes (Stegomyia)*.

Article 13.—"While specific substantive names derived from names of persons may be written with a capital initial letter, all other specific names are to be written with a small initial letter."

Article 19.—Under this article there is a Recommendation: "For scientific names it is advisable to use some other type than that used for the text." *Usually the names of genera, and lower groups, are italicized, roman type being employed for those of higher divisions.*

Article 22.—"If it is desired to cite the author's name, this should *follow the scientific name without interposition of any mark of punctuation*, if other citations are desirable (date, etc.), these follow after the author's name, but are separated from it by a comma or by parenthesis."

parenthesis."

Leach.

Article 25.—"The valid name of a genus or species can be only that name under which it was first designated on the condition:—

"(*a*) That the name was published and accompanied by an indication, or a definition, or a description.

"(*b*) That the author has applied the principles of binary nomenclature."

This is the all-important Law of Priority.

Article 32.—"A generic or a specific name, *once published, cannot be*

name is to be rejected as a homonym* when

worm which

applied to a

* A homonym is one name for two or more things; a synonym more than one name for the same thing.

Meigen in 1830. Subsequently Owen's genus was

cific name is to be rejected as a homonym when it ed for some other species of the same genus.'' m the preceding two articles that a generic name reoccupied as regards the whole animal kingdom, ne is preoccupied only within its own genus. Thus, genus ''*Pulex*,'' and only one species of *Pulex* it it would be permissible to have an *Anopheles* is, and so on for every genus of animals complain bitterly of the ''continual changing of he trouble they experience in this respect has arisen obsolete nomenclature in medical text-books and person now alive, other than those given to , should ever have heard of ''*Pediculus*'' *pubis* or this terminology was discarded on the breaking up e genera over a hundred years ago. It must be it some austere systematists fail to remember that ture were made for man, and not man for the Rules ne the less, a wise adherence to the code is the only er out of chaos Eventually, when the dozens of h have been showered on various animal parasites he happy student will have to know only one name long as the principles of nomenclature remain a are necessarily employed in a haphazard and or the reasons determining the selection of a term nor its form comprehended, and being blind our- ern if the guides whom we helplessly follow are vision.

PALUDRINE

ent to press, evidence has become available which a new synthetic anti-malarial drug marketed by the l Chemical Industries, may be expected to play a n the prevention and treatment of malaria (*See* , and 200)

aludrine acts on the asexual parasites of the human inhibiting nuclear division It has no detectable ology of gametocytes in human blood, but if mos- uman gametocyte-carrier while he is taking paludrine, iot become infected Oocyst formation fails in the cause of some action of the paludrine in its stomach. e important is the action of paludrine during the uman malaria—the incubation period of 10 days or tion of sporozoites and the appearance of clinical orms in the peripheral blood. At Cairns, in Aus- ley has shown that if 100 mg. (0 1 gramme) is given this period, sporozoite-infected volunteers, bitten

repeatedly by infected mosquitoes, fail to develop parasites in their blood. *This observation rests on the stringent test of sub-inoculating 200 c.cm. of* blood into a second group of susceptible volunteers.

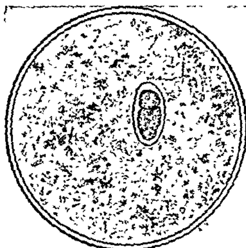
In subtertian malaria (*P. falciparum*), attacks of the disease do not follow when paludrine is stopped, the drug acting apparently as a true causal prophylactic (*see* p. 181). A single dose of 50 mg during the pre-patent phase has produced the same effect. In benign tertian (*P. vivax*) malaria, on the other hand, 100 mg. of paludrine daily acted only as a suppressive, because overt attacks followed cessation of treatment, although after a longer interval than with mepacrine given in the same way.

Therapeutic use.—*For treatment of clinical attacks the optimum dosage is not yet known.* As much as 1 g. daily has been given, but 250 mg twice daily for 7 to 14 days will probably be sufficient. This should cure patients with subtertian (*P. falciparum*) malaria; but treatment of benign tertian (*P. vivax*) relapses with paludrine has not given such good results as the 10 to 14-day quinine-pamaquin course (*see* Course C on p. 190).

Side effects.—The drug is pleasant to take and it does not stain the [illegible]

casts in the urine.

Plate 1.



Microscopical preparation showing Ancylostome Egg in human fæces
(Partly after Bass and Dock) (Wellcome Bureau of Scientific Research

Plate 2.

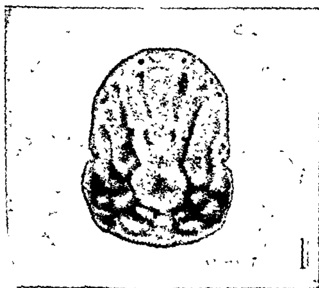
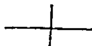
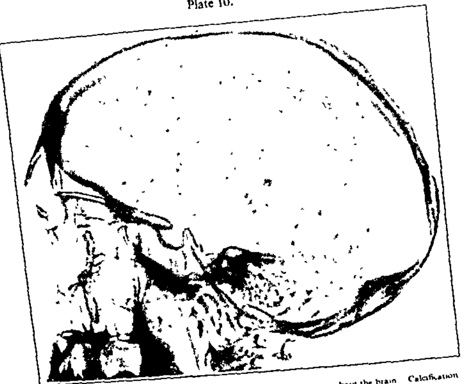


Plate 8.

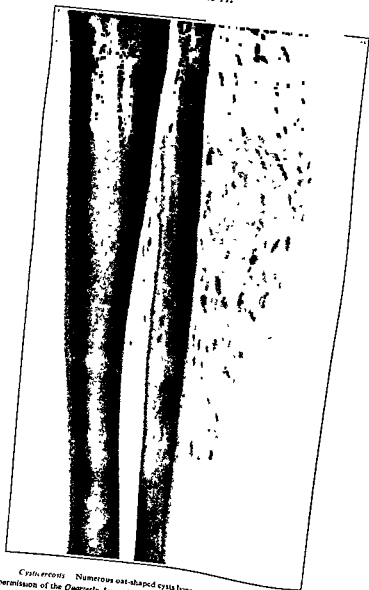


Cordylobia anthropophaga, the Tumbu Fly and its larva
(Specific myiasis-producer)
Wellcome Bureau of Scientific Research

Plate 10.



Cysticercosis Radiograph of skull showing calcified cysts scattered throughout the brain Calcification in the brain when it occurs, appears mainly to effect the scolex
...ission of the *Quarterly Journal of Medicine* and the authors, H H F Dixon and W H Hargreaves)



Cysticercosis Numerous oat-shaped cysts lying in the muscles of lower limb
(By permission of the *Quarterly Journal of Medicine* and the authors, H. B. F. Dixon and [illegible] Hargreaves.

Plate 12

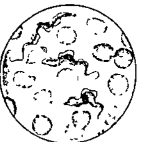


Normal jejunum



Jejunum in sprue showing segmentation and flocculation of barium meal fifteen minutes after its injection through tube. 'Deficiency pattern'.

Plate 13.



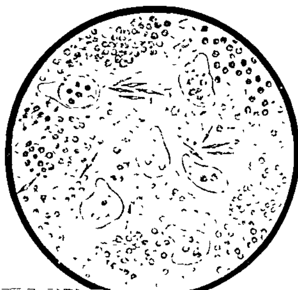
Trypanosoma gambiense, showing long intermediate and stumpy forms. (Partly after Bruce)

Plate 14.



Trypanosoma rhodesiense showing long, intermediate and stumpy forms (Partly after Bruce)

Plate 16.



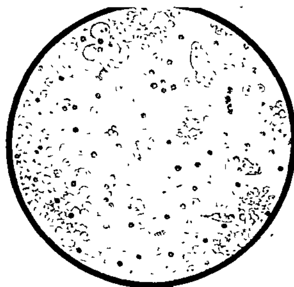
Bacillary dysentery exudate showing: Numerous pus cells, Red cells, Macrophages, which must not be mistaken for amœbæ.

ERRATUM

e caption under Plate 15 refers to Plate 16 and vice versa

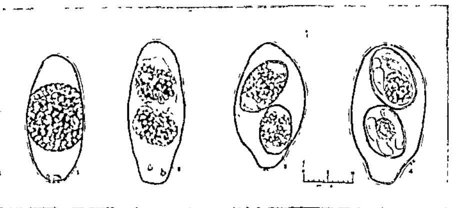
(Drawn by R M Leach.)

Plate 15.



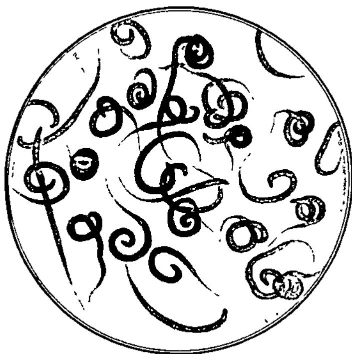
Amœbic dysentery exudate showing: Amœbæ ingesting red cells, Charcot-Leyden crystals; Bacteria.

Plate 17.



The extracorporeal development of the human coccidium, *Isospora hominis* (=*belli*) as it occurs after being passed in the fæces. On the ground or in the water the oocyst becomes infective by development as shown in Figs 1 4, producing finally within it two sporocysts each containing four sporozoites and a residual mass of protoplasm. The cysts of several species of *Eimeria*, another genus of coccidium, may be swallowed in infected fish and appear in the fæces. No *Eimeria* is known to parasitize man.

Plate 18.



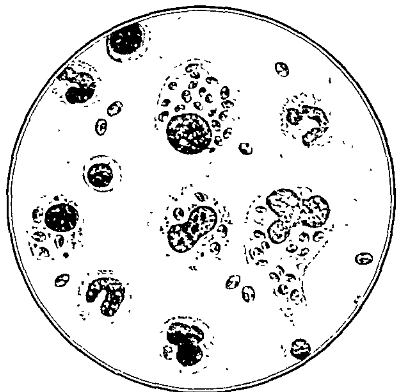
Embroys of *D. medinensis*
(Manson)

Plate 19.



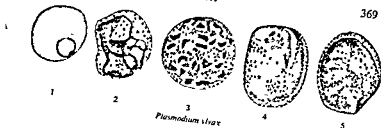
Guinea-worm lying in part superficially and being gently drawn from the subcutaneous tissues of foot. (Partly after Bahr.)

Plate 20.



Scrapings from spleen (Kala-azar) Free and intracellular parasites
(Wellcome Bureau of Scientific Research.)

A



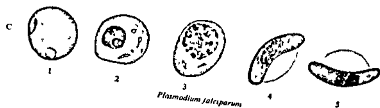
Plasmodium vivax

B



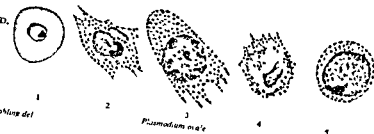
Plasmodium malariæ

C



Plasmodium falciparum

D.



Plasmodium ovale

...obling del

Malarial parasites of man. (× 2000)

1 Young ring 2 Half grown form 3 Nearly mature schizont
4 Male gametocyte 5 Female gametocyte

Plate 22.



Leishmania tropica. (After Manson)
5. Parasites in endothelial cell. 6. Free forms

Plate 23.

Cutaneous Leishmaniasis.

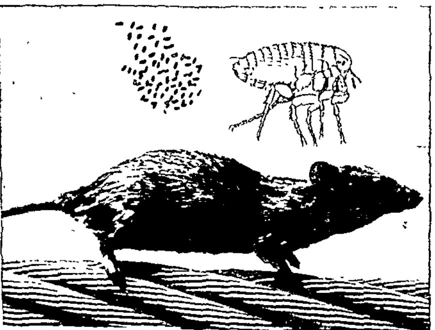
Plate 24



PELLAGRA

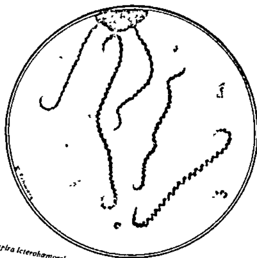
Showing the symmetrical cutaneous involvement of the distal parts of the limbs, the neck (Casal's necklace), and the face

Plate 25.



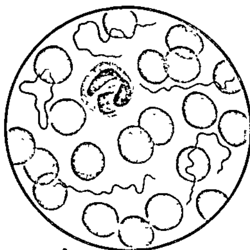
Bacillus pestis *Xenopsylla cheopis* (female) and *Rattus rattus*
(Wellcome Bureau of Scientific Research)

Plate 26



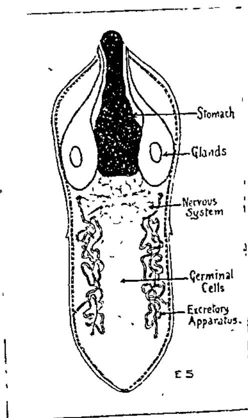
Leptospira icterohæmorrhagiæ × 3000 Modified after Hideyo Noguchi,
(Wellcome Bureau of Scientific Research.)

Plate 27.



Spirochæta recurrentis
As seen in Leishman-stained blood film of a case of relapsing fever (× 1500)

Plate 28.



Miracidium of *Schistosoma hæmatobium*

(After Sandwith)

Plate 29



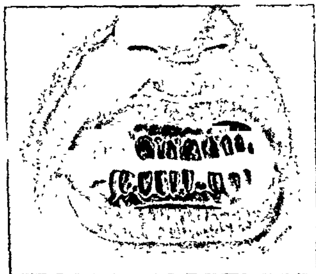


A   B

A *Planorbis boissyi*   B *Bulinus truncatus*

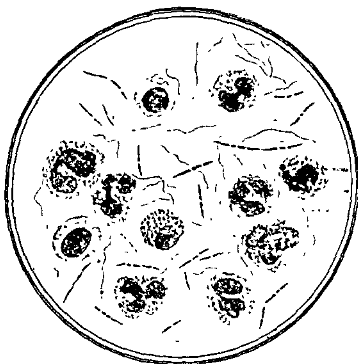
Intermediate hosts of *Schistosoma*

Plate 30.



Early scurvy showing "buds" approaching the "blossom" stages.
(Wellcome Bureau of Scientific Research)

Plate 31.



Film from *Ulcus tropicum* Smear showing Spirochætes and Fusiform Bacilli.
(Redrawn from Fourth Report, Wellcome Tropical Research Laboratories.)

Plate 32.



(A) TINEA CRURIS.—Showing typical distribution of the eruption



(B) TINEA OF AXILLA.—Note the clear-cut, slightly raised, scaling edges of the lesion. These appearances are also typical of untreated Tinea Cruris.

Plate 33.—Trichomycosis.

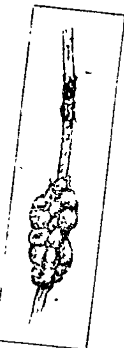


A Matted Hair, armpit

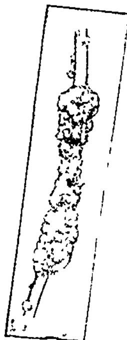


B Hair, natural size

Plate 34.

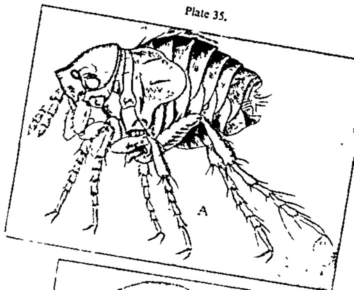


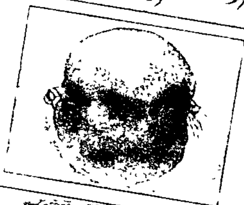


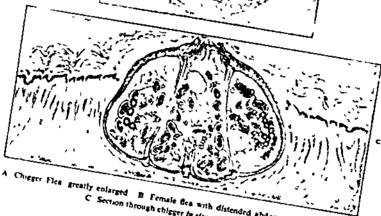


1 *T rubra* 2. *T nigra* 3 *T flava*
(Redrawn after Chalmers and O Farrell)

Plate 35.







A Chigger Flea greatly enlarged B Female flea with distended abdomen full of ripe eggs C Section through chigger *in situ* (After Karsten.)

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